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MILKSICKNESS.*†

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† This disease has been commonly known under the following names: Milksickness, Sick stomach Swamp sickness, Tires, Trembles, Slows (sometimes corrupted to Sloes), Stiff joints, Puking fever, River sickness, and Alkali poisoning. More or less fanciful and pedantic designations have also been applied to it, such as Caconemia, Colica trementia, Paralysis intestinalis, Morbo lacteo, Ergodeleteria, Mukosma Syro, and Lacemesis; none of these latter titles appears to have come into general use.

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SUMMARY AND CONCLUSIONS

THE first printed account of milksickness seems to have been from the pen of Dr. Daniel Drake, "the Franklin of Cincinnati," who published in 1810 a brief note on a "New Disease" in his *Notices Concerning Cincinnati.* This publication is now not easy of access, but the note on milksickness was reprinted by Drake in the form of an editorial addition to an article by McCall (1830). From its historical interest the note is here reproduced.

"NEW DISEASE. In the spring of 1809 Dr. Barbee, of Virginia, on returning from a visit to the Madriver County in this state, gave me some information concerning a new and formidable disease which had appeared among the settlers of that tract. Since that time I have been able to collect several additional facts respecting it from different persons, more especially Mr. Wm. Snodgrass and Mr. John M'Kag, two intelligent and respectable inhabitants of that country, who have several times experienced the disease in their persons or families. A summary of the whole is here given that physicians may determine how far it deserves the appellation of a new disease.

It almost invariably commences with general weakness and lassitude which increases in the most gradual manner; about the same time, or soon after, a dull pain, or rather soreness, begins to affect the calves of the legs, occasionally extending up to the thighs. The appetite becomes rather impaired, and in some cases nearly suspended, sensations of a disagreeable kind affecting the stomach; upon taking a little food, a greater disposition for it is generated, and more agreeable feelings are introduced throughout the whole system. Intestinal constipation in this, as in subsequent periods of the disease, exists in a very high degree. A strong propensity to sleep occurs, and according to Dr. Barbee the pulse is "full, frequent, round, and somewhat tense, but regular." During this stage exercise of any kind is highly detrimental, and if persisted in soon induces loathing and nausea at the stomach. If the patient repose upon first experiencing the symptoms, they generally cease and he is allowed a longer exemption from the *vomiting* that awaits him. Sooner or later, however, that symptom almost invariably succeeds the predisposition we have described, and either proves fatal in one, two, three, or more days, or leaves the patient in a most exhausted state from which he recovers, only to sustain, at no distant period, a repetition of the same attack.

The matter ejected is somewhat bilious, but much oftener sour, and so acrid that its action on the throat, in one case (which proved fatal), was likened to that of boiling water. Towards the close of mortal cases, it is occasionally very dark colored, so that it has been compared to that very convenient and fashionable object of similitude, coffee grounds. At this time the intestinal constipation is very great. Mr. Snodgrass knew one patient in whom it continued for nine days, throughout which he took no food whatever, and vomited during six of them. After such an attack the propensity of it is destroyed, and an uncommon degree of watchfulness is produced. The patient remains languid, and his face and person generally become rather tumid. His skin is cool, palish, and frequently affected with clamminess. He has a disagreeable burning sensation at his stomach, and hot eructations are very troublesome. The thirst is considerable. The breath is peculiarly disgusting, even loathsome. The appetite is generally poor, and the inclination to costiveness remains. These symptoms often continue for several months, during which the patient experiences frequent returns of the vomiting. But at length, more especially upon the approach of winter, they gradually wear away, leaving the patient considerably worse than they found him, and liable to a fresh attack the ensuing summer.

Nothing like *regular* periodical exacerbations is observable in this disease, no chilliness occurs, the color of the skin and eyes does not deviate widely from that of health, and gives no striking indication of bile, there is no pain in the region of the liver, nor in the shoulder, it does not terminate in dropsy, nor are there any symptoms which bespeak it a disguised or anomalous intermittent. It however prevails (though not exclusively) in aguish situations, and intermitting diseases are thought to have declined since its appearance.

It affects all ages and conditions, and both sexes, indiscriminately, except probably very young children. They, however, are not wholly exempt from it. Emigrants are not peculiarly liable to it. It was first observed in the summer of 1806, and it is thought annually to extend its geographical range and to become more intense. It sometimes commences in July or before, but oftener in August and continues till the approach of winter, when it generally but not always subsides.

The cure of this disease seems hitherto to have been left chiefly to the people, who have not yet discovered any certain method. Purging was a remedy that naturally suggested itself, and by some it has been thought very serviceable, more especially when effected by aloes; but others assert that they have frequently known a cathartic to increase the vomiting, and therefore rely more on enemata. All agree, however, that intestinal obstructions are to be overcome; and that the less the means made use of affect the stomach, the better. Vomits evidently do harm. Blisters to the gastric region are considered the most efficient remedy. Tonics have been used but no great benefit appeared to arise from them. Wine and salted meats, however, have appeared to do good, and are relished beyond anything ese. Indeed, eating a little frequently, whether an inclination exist or not, has been found a good palliative. It relieves the stomach from the gnawing which so perpetually exists. Alkaline lye has been used in one case, it gave some temporary relief, but not more than almost any other substance which might be received into the stomach. Bleeding has occasionally been resorted to, but with doubtful advantage. Ardent spirits appears to render the disease worse; it is not, however, much sought after, all inclination for it generally being destroyed.

Tea and coffee, also, with several other articles of diet, which were agreeable before the disease, are in many cases disliked for a long time after.

The disease is unequivocally observed to affect four domestic animals: the horse, the cow, the sheep, and the dog. It is often fatal to the two former, but not so fatal to the latter. It as frequently attacks horses in the winter as summer, and sometimes kills them in 24 hours.

It prevails chiefly in the neighborhood of Staunton on the Great Miami and in the county south of Madriver, between Dayton and Springfield. In these tracts ponds and marshes occasionally occur, more especially in the former. The soil and water are calcareous. The timber generally oak."

The disease seems to have existed in parts of the United States for some time before the date of Drake's note. Coleman (1822), writing of "the disease generally known by the name of sick-stomach," states that it "has been prevalent in some of the western counties of the state of Ohio, since their first settlement," and Drake (1836) gives currency to the report "that this malady was observed in some parts of North Carolina more than sixty years ago [i. e., before 1776], and that it has been an endemic in certain localities of Tennessee, Kentucky, and Ohio from their first settlement." Drake's correspondent cited in this report gives the names of two persons who died of the disease in Kentucky about 1795. McCall (1823) specifically mentions several cases occurring in parts of North Carolina between 1779 and 1800.

Lea (1821), writing of the disease in the state of Tennessee, makes the interesting statement that "as soon as settlements commenced in the county of Franklin, about 12 or 15 years since, near the mountain, many cattle were lost from some unknown poison, the nature of which is still a mystery among the inhabitants. Occasionally, whole herds were found dead in some sequestered cove of the mountains." Carney (1847) speaks of the disease being noticed, "I think sixty or seventy years ago in the Carolinas," and continues: "Upwards of fifty years since, it prevailed in Kentucky." Rawlings (1874) refers to "its first avowed recognition in the State of North Carolina—now over ninety-six years ago" (i. e., prior to 1778). It thus seems fairly clear that the disease was known in the Carolinas at least as early as 1780 and probably before that time. It appeared somewhat later in parts of Kentucky and Tennessee and a little later still in Ohio, Illinois, and Indiana. According to Rawlings (1874), Wood stated that "the disease followed emigration in its westward march from North Carolina to Tennessee and Kentucky, and prevailed in various parts of Ohio, Indiana, and Illinois." It is on record that the mother of Abraham Lincoln died of milksickness at Pigeon Creek in southern Indiana in 1818 (Nicolay and Hay, 1890).

Some writers assert that mention of this disease occurs in Father Hennepin's account of his travels, but we have not been able to find anything in Hennepin's writings that could bear such an interpretation. Dr. G. R. Thwaites who is probably the historian most familiar with Hennepin's writings informs us that he does not know of any reference that Hennepin makes to this subject.

The disease was brought more than once to the attention of early travelers in the Middle West. Faux (1823) reports its presence in Old Vincennes, Ind., in 1819, and its presence in northwestern Missouri was noted by Long's Expedition about the same time (Long, 1823). M'Kenney (1846) met with milksickness in 1827 along the Mississippi River about 18 miles above St. Louis, and Flagg (1836) gives the following historical note based on information received by him while traveling in Monroe County, Ill., in 1836–37: "A mysterious disease called the '*milk* sickness'—because it was supposed to be communicated by that liquid—was once alarmingly prevalent in certain isolated districts of Illinois. Whole villages were depopulated; and though the mystery was often and thoroughly investigated the cause of the disease was never discovered. By some it was ascribed to the milk or to the flesh of cows feeding upon a certain unknown poisonous plant found only in certain districts; by others to certain springs of water, or to the exhalations of certain marshes. The mystery attending its operations and its terrible fatality at one period created a perfect panic in the settlers; nor was this at all wonderful. The disease appears now to be vanishing."

Descriptions like this suggest inquiry into the actual prevalence of the disease in early times, and examination of the reasons for the apparent rarity of the malady at the present day.

PREVALENCE IN EARLY AND RECENT TIMES.

Many observations indicate that milksickness was of much more frequent occurrence in the first half of the nineteenth century than it has been during the last thirty or forty years. Thus Beach (1883), referring to the early period of the disease in Madison County, O., declares that he "presumes nearly one-fourth of the pioneers and early settlers died of this disease." Coleman (1822) speaks of the disease being "common and unusually fatal" in a certain district in western Ohio in the winter of 1821. Compton (1881) says: "From Mr. Thomas M. Hutchins I learn that his father settled at the old fort in Dubois County, Ind., in 1815 and that more than half the deaths that occurred in that section were from milksickness. It was also very fatal among stock." Winans (1840) contrasts the status of the disease in 1840 with his early experience: "I think it probable that I had from three to five hundred patients during the whole time the disease prevailed. It has now nearly or quite vanished away." McAnelly (1836) gloomily predicts that " . . . . some of the fairest portions of the West in consequence of the prevalence of this loathsome disease must ever remain an uninhabitable waste unless the cause and remedy can be discovered." Patton (1875) states: "When I began the practice of medicine in the year 1868 in Carter Township, Spencer County, Ind., I found in this disease the most formidable difficulty with which I had to contend." In the *Maryland Med. and Surg. Jour.*, 1839–40, 1, p. 133, is printed an "Extract of a letter from a physician [unnamed] of Danville, Ind., dated July 4, 1839" in which the statement is made that "Danville has now become a perfect charnel house; no less than fifty died of 'milk sick' during the past year, and that too out of a population of 500 inhabitants." Making all allowance for possible errors in diagnosis such assertions may well be considered ground for inferring a remarkable extension and frequency of the disease in parts of the central United States during the years of early settlement.

On the other hand, there is some evidence that milksickness was never so common or at all events so widespread as some of the above statements alone seem to indicate. Lea (1821) expresses himself regarding its prevalence in much the same terms that writers have used sixty to eighty years later: "In a particular part of the state of Tennessee, a febrile affection of a most curious nature is occasionally met with, which is of very rare occurrence." A good many of the earlier articles on milksickness were called forth by an outbreak of the disease in one family or even a single case; that such instances were deemed worth reporting is perhaps significant (see, for example, Hogg, 1842; Troy, 1861). Drake (1841) who wrote extensively on milksickness devotes a lengthy memoir to the description of a trip taken by him for the purpose of studying the disease in a certain district in Ohio in which the malady was known to prevail. Many conversations with "eye-witnesses" are related in Drake's memoir, but "No case of the disease . . . . either in man or brute was met with."[1] Sale (1871) describes the occurrence of the disease in a circumscribed location not far from Cincinnati. In this region it is said to have made its first appearance in the fall of 1818. Sale gives the following record of cases in man: 1825, 4; 1830, 6; 1834, 5; 1836, 3; 1838, 6; 1845, 2; 1856, 3; 1863, 3; 1870, 17. There are other observations that seem to support the view that the recedence of milksickness is partly apparent and is due to certain causes which will be presently specified, and that localities in which the disease may today be contracted have by no means vanished from the map. Smith (1874) of Kenton, O., in a letter to a medical journal as recently as 1874 wrote: "We are having this fall a regular epidemic of what is generally called milksickness or trembles. I have treated upwards of thirty cases." Shapard (1892) of Winchester, Tenn., expressed his belief in 1892 that the disease was then as extensive as at any time within the last fifty years. Gray (1881) in an article on milksickness notes that twelve cases of so-called gastritis, two of which were fatal, had occurred among the consumers of butter from a certain farm. Three of these had come under his own observation and were apparently genuine cases of milksickness. Gray's experience raises the question whether cases of this disease do not more or less frequently pass unrecognized and come to be reported under names such as gastritis or ptomain poisoning, thus obscuring the relative prevalence of the disease at the present time. As recently as 1907, we (Jordan and Harris, 1908) have found milksickness masquerading under the name of "alkali poisoning" in the southwestern United States where it was causing great losses among the stock and was responsible for some 38 human cases and 8 deaths in the space of ten years. According to local observers the disease has been apparently extending its boundaries in this region (Pecos Valley), a phenomenon perhaps connected with the introduction of irrigation facilities. We have also learned of the occurrence since 1900 of human cases of milksickness in Illinois in eight different localities in widely separated parts of the state, while prior to 1900 there are on record cases occurring in 17 localities.

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[1] It is worthy of note that after this expedition Drake does not mention milksickness in his extensive work on the *Diseases of the Interior Valley of North America.*

Several causes have contributed to drop milksickness out of notice and even into the limbo of things forgotten. Altho the disease is by no means extinct there are now undoubtedly fewer cases in proportion to the whole population than was the case for example in the decade 1840–50. This is partly because the disease is now and apparently always has been particularly liable to appear in thinly settled regions and in marshy or timbered grazing country never brought under the plow. It is the unanimous testimony of all observers that thorough clearing and cultivation of the land will transform a dangerous area into a safe one (Drake, 1841; Crook, 1857; Pickard, 1857; Way, 1893). Drainage and cultivation have without question reduced the total acreage over which animals are liable to contract the malady. At the same time the recognition that certain tracts of land harbor the virus of milksickness has led to the adoption of precautionary measures. In many of the old milksickness districts of the Middle West pieces of land are still to be found in which cattle are not allowed to graze, and which are often very small plots fenced off from directly adjoining fields in which animals are pastured with impunity. These tracts are usually well known locally, and all the older residents have a lively sense of their dangerous character. We have ourselves inspected a number of these areas in Illinois and have been informed of many others.

Another factor that has perhaps tended to throw milksickness into the background has been the unwillingness on the part of many writers to acknowledge the existence of a specific affection bearing this title. Milksickness is not recognized in the "International Classification of Diseases and Causes of Death," and health authorities have sometimes refused to record deaths reported under the name of milksickness while accepting the term "gastritis" as satisfactory. It is our opinion that the convenient and at present fashionable refuge from etiological uncertainty which consists in referring cases of acute gastroenteritis to "ptomain poisoning" has also been made to cover some, perhaps a goodly number, of cases of genuine milksickness. It is at least true that the symptoms that have been reported in many cases of intestinal derangement attributed to the use of milk, butter, or cheese, and that have been accredited to the ingestion of ptomains or similar poisons are very similar to the symptoms of the disease we are now considering.[1] In those regions where there is any record that milksickness ever existed, cases of so-called "ptomain poisoning" or "gastritis" should be especially scrutinized (cf. Schmidt, 1877).

All these causes, the natural inability of the practitioner who has received his medical training in the centers of population to recognize at once the identity of a somewhat rare disease found as a rule only in thinly settled communities, the definite demarcation and avoidance of the infected tracts of land in all milksickness regions, and the actual reduction in the total amount of infected territory through clearing, drainage, and cultivation, have conspired to bring about the practical disappearance of milksickness from the medical literature of the last forty years. At the same time our experience indicates that in the majority, perhaps in all, of those localities where the disease has ever been endemic larger or smaller tracts of land may be found today where there is a strong likelihood that the disease will be occasionally contracted by grazing animals dependent on the pasturage for their food supply. In these localities, under conditions to be discussed later, cases of milksickness in man also occur more or less frequently. All things considered the disease has certainly not disappeared from the once-infected localities, altho it is apparently not increasing in frequency and is probably waning.

SYMPTOMS.

a) Trembles in Cattle.—Cattle are the only domestic animals in which the symptoms have been described fully and by a number of persons. There is substantial unanimity throughout the literature. The first open manifestation of the malady consists in a listlessness and disinclination to exertion. As Drake (1841) well expresses it: "The animal begins to mope and droop, and to walk slower than its fellows, to falter in its gait." Many observers have noted also the occurrence of constipation at this stage. One of the most frequently remarked symptoms is muscular weakness and trembling which makes its appearance when the animal is driven. It was the custom in many "milksick" localities for prospective purchasers of cattle to exercise the animals vigorously before consummating the purchase in order to bring out any latent symptoms. The existence of the disease in a herd was sometimes not recognized until the animals were on their way to market. Woodfin (1878) states that "Beeves that have fattened in these infected localities, started to be driven to market, take the trembles and fail the first or second day, while other cattle feeding on the same grounds, left at home, remain healthy." Tuller (1889) has described the initial stage in the following words: "The bullock when severely affected is restless and trembles as though he was receiving a shock from a galvanic battery." Johnson (1874) remarks that cattle in this stage are often greatly excited. After describing an instance in which his own son was butted down by a steer which immediately after the attack fell paralyzed to the ground, Johnson continues: "This excited condition and disposition in cattle to fight when overheated and the consequent paralysis I have often observed." Excitability, however, does not appear to be an invariable accompaniment of the disease in cattle and is not noted by the great majority of observers.

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[1] See for example an outbreak of food poisoning described in Michigan by Vaughan and Novy, *Ptomains, Leucomains, Toxins, and Antitoxins*, 1896, pp. 104–16. Symptoms of vomiting, obstinate constipation, and subnormal temperature are reported. The farm on which the cases occurred was known as "unhealthy" and previous attacks of the same kind were said to have occurred on it.

The characteristic trembling stage passes in the most severe cases into a second stage of great weakness and exhaustion. The stiffness of the joints increases and the animal after sinking to the ground is unable to rise immediately, and may remain lying for hours or days on the spot where it has fallen. Recovery sometimes occurs in animals that have reached this stage, but death ensues in many cases.

Many observers have noted the occurrence of a foul odor in animals suffering from trembles. Thus Elder (1874) refers to the "Singular fetid odor . . . . pungent and corrosive . . . . fetor invariably attendant upon the malady, both in man and the brute creation." J. N. Smith (1837) asserts that " . . . . some of the tanners in the neighborhood can at once say, with certainty, when cattle have died of the disease, by the smell arising from the raw hides."

We had the opportunity in the Pecos Valley region in New Mexico of studying an outbreak of the disease in a herd of about 80 cattle. Approximately 25 of this number manifested definite symptoms; 2 died, 4 were killed while moribund, and 1 was killed in an early stage of the affection. The symptoms observed were very similar to those above described. The sick animals were first differentiated from the others by their lying on the ground while the other animals of the herd were standing. On being forced to rise and walk they moved slowly and with great reluctance. If driven to trot they soon slowed down. Their gait was stiff and the fore legs were sometimes carried as if the feet were sore. When an animal was continuously forced it sometimes came to a stop, began to tremble violently and sank to its knees, then awkwardly came to rest with the whole body. The behavior of the young bull shown in Figs. 1 and 2 was said by ranchmen who saw it to be highly characteristic. In another instance that we observed, an eight-month calf showed when driven the typical, enfeebled, stiff gait and muscular tremors. While shambling along awkwardly it stumbled on a prairie dog-hole and lay panting, unable to rise. When we attempted to pass a thermometer per rectum the animal struggled but was held down. The thermometer had just been removed at the end of 1¼ minutes when the animal trembled violently, took a clonic spasm in the left great muscle

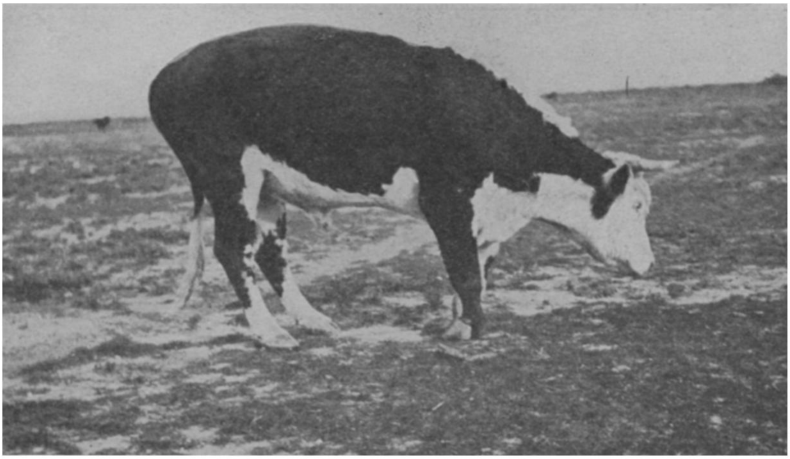

FIG. 1.—Young Hereford bull in Pecos Valley, N. M., affected by milksickness.

of the neck and breathed in great gasps; the eyes became fixt, the mucous membranes of the mouth and nose suddenly paled, and the animal died with a few slight convulsive twitchings of the legs.

Sometimes after being disturbed the animal may have a passage of the bowels, usually of a rather thin consistency, in which may be noted much mucus mixt perhaps with blood; at other times this dropping of dung is not observed and the animal may be badly constipated. From this on, if the symptoms do not improve, the animal becomes steadily weaker, rising less often, eating and drinking less and less, until it becomes so weak that it cannot rise, but lies on its side, moaning more or less frequently, its neck often becoming twisted to one side and the neck muscles standing out on the other side, hard and stiff (Fig. 3). The sclerotics are often deeply injected and accompanied by a yellowish-red discharge which becomes gummed on the canthi. McCall (1822) and some others mention that the eyes of sick cattle are "red and suffused." The breath often acquires a more or less pronounced odor of acetone, but this odor may be absent. In the later stages of exhaustion there may be twitchings of the limbs, more particularly the fore legs, less often the hind legs, so that the ground becomes grooved by the movements. For some hours or even days before death the animal may lie on its

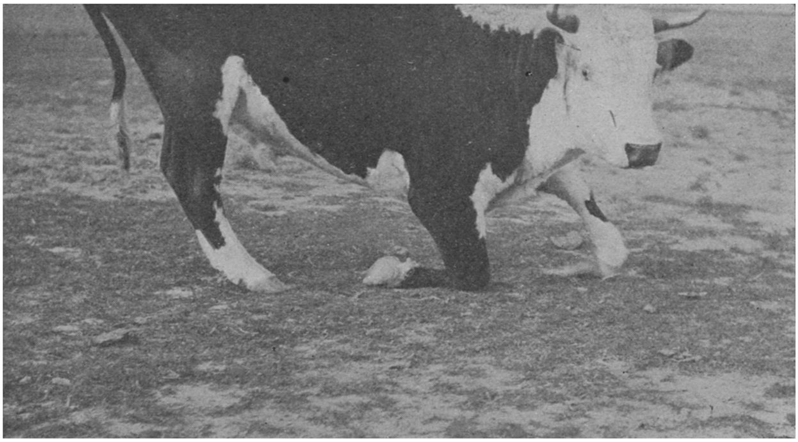

FIG. 2.—Same as Fig. 1.

side with its neck outstretched and head bent back (Fig. 4). During the midstages of the disease the temperature is irregular, often ranging a degree or two below normal. We saw no cases of paroxysmal rage manifested by any of the animals we had opportunity to study. The animal dies quietly, its breathing becoming less pronounced and fitful, developing a Cheyne-Stokes rhythm; apparently all consciousness is lost shortly before death. Feces may be occasionally passed up to within a day before death, altho as a rule the animal is more or less constipated throughout the course of the disease.

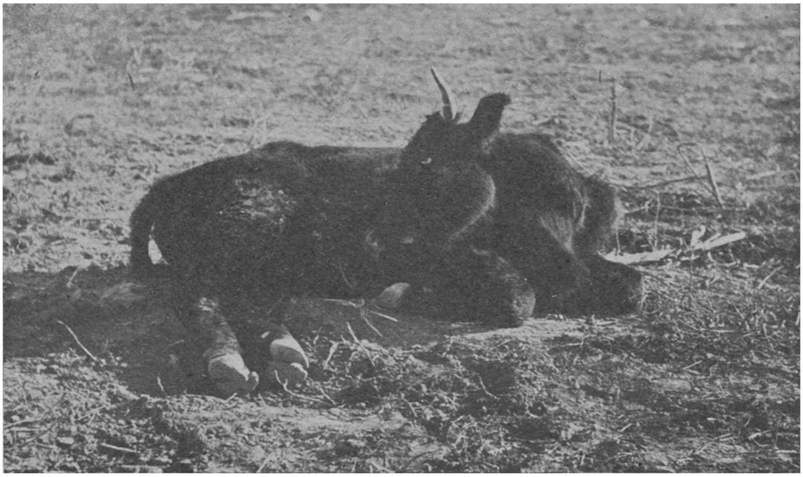

FIG. 3.—Later stages of milksickness.

b) **Milksickness in Man.**—The disease has been graphically described by a number of observers, notably Coleman (1822), Graff (1841), Byford (1855), and Way (1893). The popular name of "sick stomach" draws attention to what is one of the most typical and constant symptoms of the malady, namely, prolonged and violent vomiting. Obstinate constipation is also a practically invariable accompaniment of the disorder, and is given a prominent place in all the early descriptions. Thompson (1853) records the interesting observation made upon several patients whom he treated that "as soon as even moderately free action of the bowels was obtained, a dysenteric character was manifested in the stools." Associated with this derangement of the alimentary tract is great thirst, but the water taken is usually vomited again immediately. Prior to the appearance of these more active symptoms there is usually a period of weakness and increasing debility. Cosby (1866) states that the first stage in some instances lasts for eight or ten days before the second stage sets in. According to Logan (1849) the disease sometimes never gets beyond the first stage: "There are two forms in which we meet with the disease; the acute and subacute or chronic. To the first the name of milksickness is usually given and to the latter the appropriate title of *slows*. They are, however, the same disease produced by the same cause and each liable to be transformed into the other and differing only in degree. In the subacute form the individual is languid, unable to make any exertion of body or mind, appetite variable, bowels rather torpid, palpitation of the heart, some degree of stiffness of the limbs, trembling and sickness of stomach if any considerable exertion is made or if taking food is deferred beyond the usual time. This stage of things may exist for months after the cause is once introduced unless removed by the sanative efforts of nature or by a proper course of remedial treatment, or it may be transformed into the acute form by long fasting, fatigue, or overexertion, and in some instances

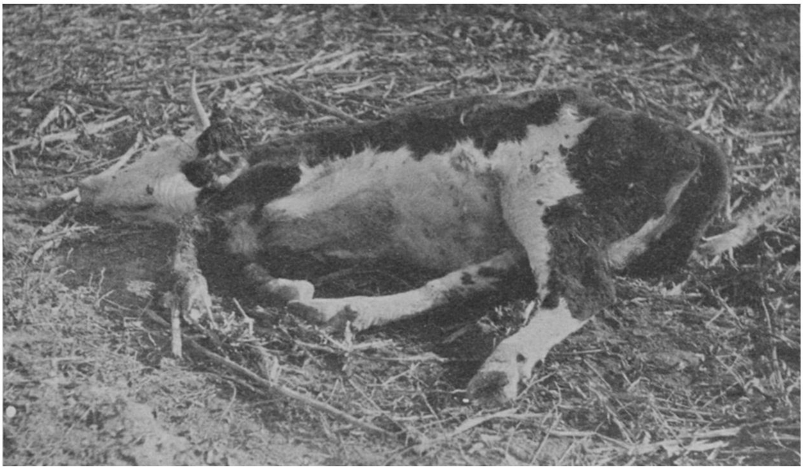

FIG. 4.—Later stages of milksickness.

by neglecting the bowels or suffering them to remain constipated for some days.

" When the disease assumes the acute form, the individual is seized suddenly with nausea, faintness, and prostration; surface and extremities below the natural temperature—sometimes cold and clammy; great distress and anxiety depicted in the countenance and the bowels almost universally constipated."

Headache is sometimes noted, but this does not seem to be a usual symptom. Coleman (1822) mentions the occurrence of "pains or soreness in the calves of the legs," and Graff (1841) and others also state that patients complain of pain in the limbs. Abdominal pain is generally entirely absent and the abdomen is flat and flaccid. Johnson (1866) thus describes the condition seen by him: "In a few hours from a healthy condition of the functions of the bowels the most obstinate constipation sets in, and so completely are they paralyzed that not the least movement of them can be observed. I have seen this condition last for a week or even two weeks without a solitary observable peristaltic movement, without pain or swelling or tenderness to pressure."

McCall (1822) and a few others state that fever is one of the accompaniments of milksickness, but the great majority of observers declare that the temperature is below normal during most of the course of the disease. Simon (1875) states that fever exists, but contradicts himself in a later paper (Simon, 1888). Way's statement may be said to represent the general consensus: "The temperature is never elevated; usually it is subnormal, ranging during the course of the disease from 97° to 98° F. At times it may be even lower than 97° F., and a return to normal or, as not infrequently happens, a slight elevation of one or two degrees above normal occurs coincident with improvement in cases that recover" (Way, 1893).[1]

Nearly all writers mention a peculiar odor emanating from the breath of the patient or observable in his neighborhood. The odor has been variously described as "garlicky," "like chloroform liniment," "sweetish," etc. Tuller (1889) in discussing this odor says: "An undertaker who has had a great deal of experience in burying those that had died of the disease, in speaking to me of this peculiar odor,

[1] See also Pusey (1880).

said it reminded him of the smell of rising bread in making milk or salt-rising bread." Byford (1855) compares it to a mixt smell of chloroform and mercurial salivation. Many writers regard the peculiar odor as a highly characteristic feature of the disease and one on which they would be willing to base a diagnosis. It seems to be essentially similar to the odor noticed in cattle (Elder, 1874; and others).

The pulse is slightly increased or may be slightly below normal; respiration is normal but becomes rapid on exertion. The urine is scanty with a trace of albumin, hiccough is sometimes noted as a distressing accompaniment of the latter stages. Eye and knee reflexes are normal.

Some writers express skepticism as to the existence of a definite affection which should be known as milksickness. Yandell (1852) who wrote rather voluminously about the matter concludes one long article with the opinion that "the various accounts of this disorder nullify each other; and the mind is left in extreme doubt whether there is anything specific in milksickness." Anderson (1867) goes so far as to assert: "I consider 'milksick,' as the vulgar call it, a mere matter of credulous fancy." Other writers such as Chapman (McCall, 1823), Thompson (1854), and Bowen (Bailey, 1868) simply declare their disbelief in the existence of milksickness. Against these *obiter dicta* are opposed the opinions of the great majority of observers who hold with Waggoner (1858) that "no one that has ever once seen a case of the disease can fail in making a correct diagnosis."

Six cases of milksickness in man have come under observation by one or both of us, two near Carlsbad, New Mexico, and four in Altamonte, Ill. None of the five resulted fatally. Through the kindness of Dr. W. E. Walsh of Morris, Ill., we have also seen several cases occurring in November, 1908, in his practice and described by him in a separate publication (Walsh, 1909). All presented some of the typical features of milksickness as recorded in the early literature, namely: (1) slow onset with rather long prodromal period of weakness and debility; (2) excessive vomiting; (3) obstinate constipation; (4) no fever, but normal or subnormal temperature; (5) slow recovery with prolonged muscular weakness and disinclination to exertion. Two of the five cases first examined, one in each group, had the characteristic odor of breath so frequently referred to in the descriptions of the disease. The odor seemed to us to be like that of acetone. The urine of one of these patients (A. McC.) was examined and gave a positive reaction for acetone (Legal's test). In the Morris outbreak samples of urine were obtained through the courtesy of Dr. Walsh and were kindly analyzed for us by Dr. R. T. Woodyatt of the Department of Chemistry in this University.

Specimens I and II were respectivly from Mrs. J. (Walsh case, No. 3) who was quite ill at the time of voiding the sample, and from Mr. J. (Walsh case, No. 4) who had recovered some few days previously from a mild attack of the disease.

Specimen I: In two containers; both samples showed the same characteristics and after preliminary tests were mixt: what follows applies to the mixt specimens.

Clear, yellow, alkalin, odor of acetone, albumin absent, reducing substances absent, acetone present as shown by the following tests:

a) Urine has the characteristic odor.

b) Urine + solution of iodin in a KI solution when treated with a strong KOH gives a strong odor of iodoform with a precipitate of characteristic pale color, which when viewed under the microscope is seen to be composed of hexagonal crystals.

c) 50 c.c. of urine diluted to 250 c.c. and treated with 3 c.c. of a 10 per cent solution of H_2SO_4, distilled until 25 c.c. only remained. The distillate smells of acetone. A small portion gives the iodoform test. The entire distillate remaining treated with a solution containing

Paranitrophenylhydrazin	3	gm.
Hydrochloric acid	0.8	"
Water	10.0	"

gives partly in the cold, completely on warming, a mass of long, fine, silky, golden, thread-like crystals which after washing in cold water and drying over H_2SO_4 show a melting-point of 148° C. accurately.

Another portion of this urine was similarly treated with H_2SO_4 and distilled. The distillate was then made alkalin and redistilled gave the same results as in the foregoing. (This proved the neutral character of the substances isolated in both instances as opposed to, say, formic acid which is also present in the urine of this case.) The crystals correspond to the paranitrophenylhydrazone of acetone (see Bamberger and Sternitzki, *Ber. d. deutsch. Chem. Gesellsch.*, 1893, 26, p. 1306).

From 50 c.c. of the urine was recoverd 0.25 gm. of the hydrozone; this corresponds to 0.083 gm. of acetone, equivalent to 1.6 gm. per liter of the urine, i. e., a total daily output of 2.4 gm. supposing that the patient had passed 1,500 c.c. of urine of the same kind as the specimen examined.

d) The urine also shows with Fe_2Cl_6 a marked "bordeaux red" coloring which disappears with heating and with mineral acids (e. g., HCl). Heating the urine for five minutes at the boiling-point before applying the test practically destroys the test, especially after making the urine acid. The color fades spontaneously when the test has stood for a few hours: result, *aceto-acetic acid.*

e) *β-oxybutyric acid.*—A sample of the urine saturated with ammonium sulfate and made acid with H_2SO_4 (10 per cent solution), then shaken with ether several times; the ether evaporated and the residue taken up in water and polarized shows marked levo-rotation of 0.7 degrees. The unconcentrated urine also shows a levo-rotation of 0.22 degrees.

f) Indican, phenol, etc., not found in increased amount above that found in ordinary clinical tests.

Specimen II: This sample presented the following characteristics: alkalin, heavy deposit of phosphates, no albumin, no reducing substances, no surely demonstrable acetone, no aceto-acetic acid or other abnormal constituents.

An incomplete examination of urine of fatal case H. J. (Walsh case, No. 2) showed:
Albumin—none.
Reducing substances—none.
Acetone—odor, and iodoform test positive.

In six of the seven cases reported by Dr. Walsh a sweetish odor was noted in the breath. Several of the patients complained of pains in the calves of the legs and in the joints, and also of burning epigastric pain. One case showed a brief period of active delirium. In these cases the liver areas were percussed out, and in two the liver was found projecting below the margin of the ribs (2.5 cm. and 4.5 cm. respectively). In the third case (convalescent) the liver could not be felt below the margin of the ribs, but the attendant physician informed us that enlargement of the liver had existed prior to our examination. Dr. F. F. Doepp of Carlsbad, N. M., who has attended a good many cases of the so-called alkali poisoning has stated to us that the liver is enlarged in all cases seen by him. One of the striking features in all the cases we have observed was the very great exhaustion and muscular weakness which persisted far on into the convalescent stage. Great stress is laid on this feature in the descriptions of early writers.

c) **Other Animals.**—Besides cattle, many other domestic animals are said to be affected with a disease resembling trembles. The symptoms, for the most part, are not given with any degree of fulness, but are described as "similar to those of the disease in cattle." Horses, sheep, goats, and dogs are all said to suffer from the disease under natural conditions. Hogs are declared by some writers to be susceptible to the disease (McCall, 1822; Drake, 1840; Davis, 1881; Coleman, 1822; Winans, 1840) while by others they are asserted to be rarely affected or entirely immune (Woodfin, 1878; Johnson, 1866). The available evidence seems to be in favor of the view that hogs are not as liable to contract milksickness as other domestic animals, but that nevertheless they are not under all circumstances exempt. Chickens, buzzards, vultures, and crows are also said to be affected by feeding on the carcasses of animals dead from trembles.

Statements are made that various wild animals are sometimes affected. Among those mentioned by several different writers are deer, wolves, and foxes.

McCall (1822) describes with some detail the disease in a dog: "I saw a dog pass through every stage of the disorder. He had fed on the flesh of a calf which died by sucking its mother's milk. The dog coming home with some putrid flesh upon him, I suspected what he had eaten and watched him. He appeared to be in a state of great anxiety—went to a spring for water and then returned to the poisoned carcase. Calling him he came to me manifestly very sick. On the way he ate some grass and vomited. After getting home he concealed himself under a floor where he lay all the ensuing day. His eyes became fiery red, and a peculiar hoarseness marked his barkings. He remained in the same condition next day, refusing every kind of sustenance except water. His whinings were almost continued, and he seemed intent on biting whatever came within his reach. The next morning I found him dead."

A good many other writers mention the susceptibility of the dog, but give no description of symptoms (Sykes, 1891; Woodfin, 1878; Davis, 1881; Buck, 1840; Johnson, 1886). A suggestive note is made by Travis (1840) to the effect that his "own dogs have had the disease in such a manner as to render them unable to walk, by feeding on a dead cow." Drake (1841) says that affected dogs drop dead when fighting or running.

We have ourselves seen no dogs naturally affected with the disease, but we have been informed by reliable witnesses in and about Carlsbad, N. M., that dogs have been sometimes observed to sicken and die after feeding on the carcasses of "alkalied" animals. It is, however, certain that the flesh of such animals will not invariably communicate the disease. In New Mexico we several times made the experiment of feeding dogs with considerable quantities of meat (thigh muscle) from animals dead of typical trembles, but in no case did we succeed in producing any symptoms of illness.

We have not ourselves seen cases in sheep, but the following notes were made for us by Mr. D. D. Todd, Fellow in Bacteriology, who under our instruction investigated an outbreak of the disease in sheep in Tiro, O., in June, 1908.

Lamb 1.—Male, age 10 weeks. The animal when first seen was lying on its side, made no attempt to get up, and did not resist being handled. It showed no sign of pain, but occasionally ground its teeth. The eyes were clear and there was no injection of the sclerotics. Axillary and inguinal glands were not palpable. Breathing was regular, 28 per minute; pulse, 118. Some mucus in nose.

Lamb 2.—Female, age 10 weeks. This animal, unlike the first, often struggled to get on its feet, but was unable to rise. It would after struggling keep its legs and feet going in a walking motion for some seconds. Breathing was forced and jerky, but regular, rate 33; pulse, 111. Autopsies were made on both these animals (see p. 449).

We have seen one horse (in New Mexico) which may or may not have been a representative case. We were informed by ranchmen, however, that "alkalied" horses usually showed the symptoms observed in this animal. This animal had been out on pasture land on which two other horses had contracted the disease and had died a day or two before this animal was seen. The horse stood in its stall, legs somewhat wide apart, and motionless except for its somewhat rapid breathing, sweating profusely about the head, neck, and shoulders, back, and flanks. Its head hung low and the animal appeared to be fully conscious. Its breath possessed a faint odor of acetone. Its rate of breathing was 28 a minute and its pulse 72. On percussion, the lung note was fairly clear and no sign of any pneumonia or bronchopneumonia could be discerned. Auscultation was rendered difficult and untrustworthy by the squeaking of the hair on the hide during the breathing, but no blowing note or coarse rales could be made out. No muscular tremors were noticed while the animal stood in the stall. The feces which had been passed were well formed and did not look abnormal. The animal died at midnight the next day after having been ill about 72 hours. It is to be regretted that no autopsy was obtained on this animal but circumstances rendered this unavoidable.

INCUBATION.

By far the majority both of isolated cases and family outbreaks of milksickness are described as ushered in by a period of indefinite length during which the patients "did not feel well." Williams (1863) expresses the general belief when he states that "for several days previous to the attack the patient has a general feeling of indisposition." According to Way (1893) the onset of milksickness is never sudden or violent. In a few instances a definite period of incubation has been supposed to precede the appearance of violent symptoms. Beach (1883) records what he considers a case of probable incubation of two days and Cosby (1866–67) one of less than 36 hours. Buck (1840) reported a unique family outbreak, Case I developing "in September," Case II on October 17, Case III on October 19, Case IV on October 21, and Case V (Buck himself, the attending physician) on November 10. The second, third, and fourth cases were in persons associated with or attending upon the first. If it be granted that these cases were really cases of milksickness, which seems somewhat doubtful, the instance stands practically alone, since other recorded family epidemics indicate simultaneous or nearly simultaneous infection of the different members and there is no evidence pointing toward contact infection. Spalding (1881) notes one instance of an interval of three days and another of six days between the discontinuing of suspected milk and the onset of symptoms. McCoy (1907), who investigated a recent epidemic in Tennessee, altho able to establish the date of infection with a high degree of probability, could not learn the exact dates when symptoms appeared except in the case of one guest in whom they appeared "about ten days after he had taken breakfast at the house."

A number of writers have put on record cases where intoxication rather than infection seems to afford the most plausible explanation for the sudden onset of the symptoms. Most of these are attacks of disease attributed to the use of meat, altho McCall (1822) states that symptoms appear "in a short time" after swallowing milk. Coleman (1822) personally observed "an instance of a whole family becoming sick with this disease, some of them in a few hours after dining upon a loin of veal, in which it was afterwards satisfactorily ascertained that the calf labored under the disease at the time it was butchered." Lewis (1829) mentions one family outbreak in which 17 persons were "all attacked with the same disease in a few hours after using the milk of cows which had fed in a milk-sick district of country, some more and others less violently." The same writer records another case where immediate effects followed the eating of steak; "Mr. T. expired at the table while eating (!), his wife soon after." Drake (1841) advances the following somewhat doubtful evidence: "In the month of July last, about twenty of the boarders, in the hotel of Mr. Madeira, Chillicothe, O., were attacked, in one, two, or three hours after breakfast, with nausea and vomiting. . . . . Of course, this affection was ascribed to something eaten at the table, but the only article taken by the whole was butter; and that butter, it was ascertained had been brought from an adjoining county in which the milksickness prevails." Still more dubious, perhaps, is the outbreak of food poisoning reported by Barbee (1840): "In March, 1838, a family of six persons, traveling westward, put up at a house a few miles east of Terre Haute, Ind. At breakfast they all partook freely of *butter* and *milk* and departed immediately on their journey. By the time they reached Illinois, in five or six hours, they were all taken with nausea, vomiting, etc., and died, every one of them, in from two to six days. Upon inquiry it was ascertained that the place where they had taken their breakfast was in a 'milk-sick' region." There is no convincing evidence that either of these outbreaks had anything to do with milksickness. Sale (1871) enters into greater detail: "A young calf took the trembles and died; the cow was milked and the milk fed to two pigs that were in a pen; these pigs thrived and fattened, and in due time were slaughtered. The first meal that the man and his wife (owners of the pigs) took made them sick and they both died in four days after eating the pork, with all the symptoms of milk sickness. *Neither cow nor pigs showed any signs of the disease.*" Altho recorded more circumstantially it should be noted that the instance quoted was not put on record until twenty-five years after the event (1845).

Some of the most definite symptoms of milksickness are lacking in these instances of sudden onset, and while it is possible that the ingestion of poisonous compounds formed by *B. lactimorbi* may account for some of these outbreaks, it may be questioned whether such cases do not in part belong to other varieties of food poisoning. Our own experience has been entirely with cases showing a longer or shorter period of *malaise* prior to the appearance of severe symptoms. In one of the New Mexico family epidemics we have obtained a full and clear account of the circumstances surrounding the outbreak from an observer of good judgment who was himself one of those who suffered from the disease (A. M. H.). There seems in this case reason to suspect the flesh of a calf slaughtered about December 1, 1906. So far as can be gathered active symptoms appeared in four different individuals within 7 to 10 days after beginning to partake of the meat of this animal, and a fifth case had "a touch of the sickness" about four weeks later. In each instance a period of indisposition preceded the attack. In the Altamonte, Ill., outbreak studied by us, we were informed that the four youths who were affected had been feeling "out of sorts" for about a month prior to the onset of violent symptoms. In this outbreak, as in many others, infection was probably more or less continuous over a considerable period. Similar conditions prevailed in the Morris, Ill., outbreak (see p. 416, also Walsh, 1909).

RELAPSES. IMMUNITY.

One of the most characteristic features of milksickness is a tendency or at least a liability to relapse or exacerbation. Logan (1849) states that the subacute forms of the disease "may exist for months" or "may be transformed into the acute form by long fatigue, fasting, or overexertion and in some instances by neglecting the bowels or suffering them to remain constipated for some days. Especially if the patient takes vigorous exercise during convalescence the symptoms are apt to recur. Reagan (1884) expresses the general consensus when he says, "It (the poison) lies quiet in the system for a long time without exhibiting any of its toxical powers until the person or beast is forced to take exercise." Genuine second attacks are, however, reported. McAnelly (1836) records an instance where a farmer and his wife were attacked by the disease "every summer," and adds, "I was called to see them in August, 1833, in their fourth attack and I do not recollect ever having seen a more violent one." Spalding (1881) mentions a case of man and wife who had a first attack in April, 1876, and a second in July, 1878, and refers to another instance of a second attack 10 years after the first. Gray (1881) also reports an instance of relapse. Jones (1852) cites the following remarkable case as occurring under his own observation: "A Mr. Taylor and his family, who had contracted the disease in a 'milk-sick' district in the mountains of North Carolina, and who had been relieved afterwards, settled in the neighborhood where I was born (southwestern Virginia) where 'milksickness' was never known to prevail for many miles around. They remained in the neighborhood and appeared to enjoy excellent health for about two years. In the autumn of the second year, the father, mother, and two brothers were again seized with symptoms of 'milksickness;' the disease assumed a violent character . . . . [all died]. Not another case occurred in the whole county either of man or beast."

We have had no personal experience of successive attacks in human patients, but all observers with whom we have talked are agreed that the liability to relapses is one of the marked features of milksickness. Dr. F. F. Doepp of Carlsbad, N. M., who has seen a number of cases of the disease[1] during the last 10 years, informs us that recovery is usually slow and that if great care is not used the patient is likely to suffer a relapse, especially after overfeeding or overexertion.

It is the unanimous testimony of stockmen that cattle do not acquire immunity from an attack of this infection. We ourselves saw one fatal case in a heifer which was said by the owner to have shown symptoms of the disease the preceding year.

MORTALITY.

Statements in regard to the mortality differ greatly. Coleman (1822) asserts that "about one case out of twenty or thirty is lost of those who experience the disease in its active form." Allen (1878) places the mortality about twice as high as Coleman. Hibberd (1844) thinks the mortality about 2 per cent of the whole number attacked and about 5 per cent of those claiming medical assistance. Tuller (1889) estimates a mortality of 10 per cent, while Collins (1902) says, "I find that about 40 per cent of my cases in which I am reasonably certain of the diagnosis have died."

The list on p. 425 gives those instances we have been able to collect in which the number of cases and deaths is specifically stated.

Through the kindness of Drs. Friedman and Doepp of Carlsbad, N. M., we have obtained a record of 38 cases and 8 deaths occurring in and about Carlsbad in the period 1898–1908. We have also been informed in a personal letter by Dr. R. J. Boatman of Carlsbad of 7 cases and 2 deaths that occurred in his knowledge in Nashville, Ill., in 1864. Of 4 cases investigated by us in Altamonte, Ill., in 1908 none resulted fatally. There was 1 fatal case and 6 recoveries in the Morris, Ill., outbreak in 1908. Adding the cases obtained by us to the numbers given below, we have a total of 318 cases and 75 deaths or a mortality of about 20–25 per cent.

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[1] Locally known as "alkali poisoning."

Cases	Death	Authority
4	2	Lewis (1829)
10	5	Carney (1847)
1	0	McNutt (1847)
49	26	Sale (1871)
50	7	Smith (1867)
30	0	" (1874)
3	2	Houser (1880)
22	4	Spalding (1881)
3	1	Gray (1881)
4	2	Simon (1888)
11	6	Pusey (1880)
6	5	Graff (1841
9	5	Tuller (1889)
2	0	Scott (1889)
6	1	Hurd (1875)
13	2	Sykes (1891)
6	1	Lyday (1896)
9	1	Michigan S. B. H. (1897)
5	2	Collins (1902)
13	6	Palmer (1904)
6	6	McCoy (1907)
262	64	

There is no doubt that the real mortality from the disease is much lower than this. Many of the cases reported are in family outbreaks which attracted notice from their severity, and it is undoubtedly true in this as in many other diseases that the milder or "abortive" cases are regarded as less worthy of report and often do not come to the notice of physicians at all. We believe it safe to assume that the mortality from milksickness does not exceed 10 per cent and may be considerably lower.

SOURCES OF THE DISEASE.

a) **In Cattle and Other Grazing Animals.**—All observers are practically agreed that cattle pastured on particular tracts of land acquire the disease, while at the same time others on adjoining pastures never show any signs of illness. A few illustrations may be cited from the voluminous literature.

"A farmer on the high and dry land near Annapolis, Ind., was in the habit of keeping a portion of his cattle overnight in a small lot, in which was no water and but little vegetation. Those cattle were attacked with sloes or milksickness, while the cattle on other portions of the farm were exempt. He excluded his cattle from the lot, and the disease never occurred on the farm afterward" (Wilkinson, 1857). Shelton (1836) relates an instance where by fencing out live stock from a suspected tract of ground the disease was suppressed for eight or nine years. Then, "the enclosure having decayed and fallen down," the disease again manifested itself "and rarely fails to occur in animals that feed long on the spot." The same writer states that "in Blount County, Tenn., there is a locality embracing not more than ten or fifteen acres, on which the disease has been known to originate for nearly, perhaps quite, forty years." Drake (1841), as the result of an investigation of the conditions under which the trembles occurred in southwestern Ohio, drew the following conclusions: "We feel warranted, then, in deducing and resting upon the following conclusions: (1) That in *this district*, the trembles in cattle, horses, sheep, and hogs, are produced by their frequenting the densely timbered table-land, which from its flatness abounds in wet places and ponds, indicated by the presence of lofty white elms, black walnuts, maples, burr oaks, and other trees, which delight in a rich and moist soil; (2) that when the same animals frequent prairies, barrens, and the hill-lands, near the larger streams, although they may be heavily timbered, they do not contract it; and consequently, its cause does not exist there, or at least is not efficient."

Crook (1857) asserts that, "In no instance has it ever been known in this county [Spencer County, Ind.] during any other than the grazing season, and then *only* upon lands that had never been in cultivation." Many other writers claim that stock kept on tame or cultivated pastures never contract the disease, and that only wild lands can give rise to the affection (see Bennett, 1822; Pickard, 1857; Simon, 1888; *et al.*). Walker (1886), however, relates the following case: "Dr. W. S. Sims of this place tells of a farmer in Hamburg Township, Jackson County, N. C., who has a half-acre lot enclosed with his dwelling. In this enclosure are fruit-trees and some of the native grasses, and the place has been under cultivation for twenty years or more, and yet whenever cattle are turned upon that lot during grazing season they are sure to die with the disease in a few days." The explanation of this apparent exception or anomaly is perhaps given by Shapard (1892) who declares: "I am not alone in the opinion that there are fields in this county [Franklin County, Tenn.] that have been in cultivation a long while, perhaps 50 years, in which the farmer does not feel entirely safe in allowing his cattle to roam or graze at certain seasons of the year." In such cases Shapard believes that the persistence of the disease on cultivated lands is due to the existence of some strip of woodland, rocky knoll, or fence corner, which has not been reached by the plow.

There is little or no doubt that clearing, drainage, and cultivation of land greatly diminish if they do not altogether do away with the liability of grazing animals to contract trembles. The connection between a special locality and the occurrence of the disease is in any case well established. Sawyer (1867) expresses the general opinion when he asserts, "It does not appear to extend its limits, but where it now is it *always existed*." And there is practically no observer of this disease who would not agree with Nichols (1876) when he says, "I can point to a certainty to every district or farm where this disease does or does not prevail."

The complete exemption of certain pasture lands whose topography and vegetation are apparently identical with those of the "milksick" areas has led many to believe that the disease is closely associated with the soil itself. This opinion is strengthened by such observations as those of Allen (1878), who writes: "There are certain localities in that county [Effingham County, Ill.] where cattle resort for the purpose of licking. They lick large holes in the earth and when that is the case many of them die of the disease."

Our own observations completely confirm the existence of a connection between this disease and particular soil areas. We have seen in New Mexico and in Illinois adjoining tracts of land apparently identical in topography and vegetation, the sole discoverable difference being in their ability to cause trembles in grazing cattle. Many small pieces of pasture land in the Middle West remain to this day fenced off from the rest of the farm on account of their dangerous character, demonstrated or suspected. Some of the cases of milksickness in man reported in recent years have followed the change of ownership of "milksick" farms and the disregard by the new owner of the warnings given him by better-informed neighbors. In all instances the localization of the disease has been one of its most striking features.

Not only soil in particular localities but water has been suspected of harboring the exciting agent. Beach (1883) mentions an instance where cattle contracted the disease after eating hay from a meadow that had been overflowed with water draining from a tract of land notorious for producing trembles in grazing cattle. Lyday (1896) states as an uncontroverted fact that (in North Carolina) "the disease is sometimes contracted by drinking the water of the streams which run out of the 'milk-sick' coves." White (1836) gives several specific examples, not, however, any too well authenticated, of outbreaks among sheep and cattle attributed to drinking-water. Fulton (1884) records the following cases in which water seemed the probable or only possible source of the disease. After quoting some hearsay evidence, he says: "Many similar instances could be cited, some two or three of which have fallen under my own observation. One in Richland Township, Logan County, O., where the cattle had been taking the disease from the first settlement of the country, and several persons on that and adjoining farms had taken it, and most of them had died, until a spring was finally suspected and inclosed—since which time to the present, some fifteen years, there has been no more of it.

"Another, that of a low, marshy piece of ground in Brunswick Township, of the same county, the country around which was notorious for the number of cattle that died of the disease, and of persons that took it, until, with the improved agriculture of the country, that place, with other low lands, was ditched and drained; since which time there has been no more of the disease in that neighborhood in either man or beast.

"Another instance, that of a stock-well on a farm in Clark County, as I am informed by several credible witnesses, from which the cattle were accustomed to be watered, and had been taking the disease for a number of years, when it was suspected and closed, since which time there has been no more of it.

"Again, there is a farm in Hardin County, on which members of every family that has ever lived there have had the disease. On that farm I have attended patients who said that they had not used meat, milk, butter, or cheese for weeks, guarding against the disease. The presumption therefore was that they, and also those of the previous families that had lived there, had obtained it directly from the water." No attempt to discredit the evidence for occasional water transmission appears to have been made, altho Tuller (1889) states that he has never known the disease in cattle or man to be caused by drinking-water.

b) In Man and Other Animals.—The circumstance that has given this disease its name of *milksickness* is well authenticated. There are numberless instances on record where the use of milk from particular cattle has been followed more or less promptly by the characteristic symptoms of the malady. Some of these have been already cited (p. 421). Townshend (1883) describes the following family outbreak which came under his own observation.

"Of a family of six persons, attended by the writer, five, who had used the milk of the same cow, had Milksickness; the sixth person used neither milk nor butter and escaped entirely. At the time of the illness of this family a yoke of oxen belonging to them were sick of trembles and both died. The cow which furnished the milk used by the family and which had pastured with the oxen was at the time severely sick, but finally recovered."

McCoy (1907) has recently reported a somewhat similar case in Marion County, Tenn., "So far as could be learned the cow responsible for the outbreak had obtained access to what is locally known as 'poison ground' about the 10th of April.

"The milk from this cow was used regularly, and apparently without bad results, until April 25.

"In addition to the five members of the family, there were two guests at breakfast on that day. Of the seven persons who ate breakfast on that date (April 25) all used milk and butter, with the exception of the mother of the family, and all who used the milk and butter became sick and died."

Other writers presenting more or less cogent evidence of the causation of the disease from drinking raw milk are McCall (1822), Lewis (1829), Barbee (1840), Logan (1849), Philips (1857), Cosby (1866), Nichols (1876), Woodfin (1878), Sykes (1891), and Beck (1905). In fact there seems to have been no doubt in the minds of all the early settlers that milk was the article of food clearly incriminated. Instances of this belief are found in the works of early travelers through the West as well as in medical journals. M'Kenney (1846) relates the following experience: "A settler came to my encampment (1827) [about 18 miles above St. Louis, on Mississippi River]. I asked if he could supply me with some milk. He answered, 'We don't use it.' I asked why. 'The people,' he replied, 'about these parts, were afraid of the *milk-sick;* and never used milk after early spring. They do not even permit the calves to suck it; if they do, the calves die, as well as the people.' "

Long (1823) makes a somewhat similar statement. It has already been pointed out that in nearly all the districts in which milksickness has been observed the cattle suffer from the malady known as trembles or slows. An anonymous writer in the *Western Medical Gazette* (1832) expresses the prevailing opinion when he writes: "I have never known nor indeed ever heard of the milksickness prevailing where the cattle were not subject to the trembles." While this seems to be generally true there are some alleged exceptions which will be considerd presently. Our own observations upon the connection of milk with the disease in man are limited to an outbreak in Altamonte, Effingham County, Ill., in the summer of 1908.[1] Four cases of the disease appeared in a family of ten living on a farm known from the days of earliest settlement to give rise to milksickness. A particular spring and the creek fed from it had long been suspected as the source of infection in cattle. The disease, however, had not been known to occur in early summer, and cattle were accordingly usually pastured on that portion of the farm where the spring was located. They were kept there in 1908 in the early season until about June 22. About 10 days later acute symptoms of milksickness made their appearance. The whole family partook regularly of the milk, cream, and butter derived from these cows that had been pastured in the neighborhood of the suspected spring, but those individuals that manifested symptoms[2] were said to have taken particularly large quantities. Both parents escaped altogether; the elder daughter who had remained well had been away from home prior to the outbreak; the younger daughter was said to have taken little milk or butter; a boy of nine remained entirely well and a child of two and one-half years showed no characteristic symptoms, altho vomiting had occurred while the others were ill. The cows were to all appearance entirely healthy, and showed no signs of disease before or after the outbreak; a six to eight-weeks-old calf whose mother was one of the animals providing the milk used in the family also seemed in the best of condition. A cat that was being fed on the milk from these cows was itself well, but lost all its eight-weeks-old kittens, five in number, during the outbreak in the family. A dog receiving milk from the same cattle showed signs of illness and was noticed to vomit repeatedly. The vomit was a clear watery fluid; no acetone odor to the breath of the animal could be detected.

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[1] We are under obligation to Dr. F. Buckmaster of Altamonte for notification of this outbreak and for other kind and effective assistance.

[2] Four young men, aged, respectively, 22, 20, 16, and 14.

In the Altamonte outbreak it was not possible to differentiate between butter and milk as possible factors in causing the disease. Butter, however, has been regarded as in itself capable of causing milksickness. Johnson (1866), Scott (1889), Beck (1905), and others speak of the agency of butter in the production of milksickness as if it were well demonstrated. Gray (1881) records 12 cases of "gastritis," believed by him to be milksickness, which occurred during the space of six years in families using butter made on a particular farm. Beach (1883) records a specific case in which the patient "ate some butter on his bread, but no cheese, milk, or meats of any kind." Nichols (1876) makes the statement that "man receives this poison through milk, cream, or animal food and *never* by butter," but later in the same paper adds the interesting qualification that "butter may produce trembles if churned from sweet cream, otherwise it never does."

Any doubts that we may have had about the relation of butter to this disease were set at rest by an outbreak coming under our observation at Morris, Ill., in November, 1908.[1] This, like most of the recorded cases, was a family outbreak, a fact that in itself goes far to fasten suspicion upon some particular article of food or drink. At the time the cases appeared (five in a family of six), there were no other cases of the disease in the immediate neighborhood. The eldest son of the family (J., 17 years) was employed on a farm (P.) about six miles from Morris; this young man brought butter from the P. farm to the J. family, but no milk. The butter was churned from the milk of cows that had been allowed to forage during the fall of 1908 in some woods long known as a locality in which grazing cattle were likely to acquire trembles and in which eight cattle had contracted the disease and died in 1906. At the time of

[1] We are greatly indebted to Dr. W. E. Walsh, of Morris, who kindly notified us of this outbreak and has assisted us in its study in a variety of ways.

the present outbreak the cows on this farm showed no signs of illness. About three weeks before the cases developed in the J. family, two young men on the P. farm had complained of feeling "out of sorts" and very weak; one of them "could not climb into a wagon;" this lad about a month later, and after the J. cases in Morris had recovered, came down with a typical case of milksickness apparently as the immediate consequence of a hard day's labor husking corn. In this patient there was present the typical acetone odor to the breath and urine as well as other characteristic symptoms of milksickness. It may be added that the youth J. who worked on the P. farm and, like the P. sons, drank the milk of the P. cows, remained free of any symptom of illness. Two or three hogs, however, fed with milk from the suspected cows, are said to have died with symptoms resembling those of trembles.

There seems little doubt, therefore, in view of all the facts, that butter brought from a "milksick" farm was responsible for the cases in the J. family in Morris. It should be remarked that in this outbreak as in many recorded in the early medical journals the milk and milk products of animals themselves apparently healthy proved capable of giving rise to fatal illness in man.

It has been supposed that, in addition to butter and milk, cheese is sometimes the source of milksickness. Some writers (e. g., Scott, 1889) refer to cheese as if it were a generally recognized carrier of the specific poison, but we have yet to find any particular instance in which the epidemiological relation of cheese to milksickness is clearly made out.

On the other hand the flesh of animals is definitely implicated as the bearer of the disease-producing agent. Carnivorous animals are alleged by many writers to acquire the disease from feeding upon the carcasses of animals dying from trembles. Many of these statements seem to be based on direct, first-hand observation (see, for example, Coleman, 1822; De Bruler, 1858). Dogs, pigs, and wolves and also fowls, buzzards, and crows are asserted by numerous observers to contract the disease in this manner. Specific instances of the causation of the disease in man from meat-eating are given by Coleman (1822), Lewis (1829), Sale (1891), and others. Conner (1904) records the case of his father who died of milksickness when he himself was eight years old. "My father and two companions took dinner in a restaurant in Springfield, eating fresh beef, and in a few days two of them were dead and the other almost dead, recovering after a lingering illness." McCall (1830) cites an outbreak where some sheep died from trembles and were eaten by hogs which in time perished from the same malady. The carcasses of the hogs were burned except one which was accidentally overlooked and was picked by chickens. The chickens were used for food and were supposed to have caused milksickness in five persons, two adults and three children; one son "who ate none of the chicken or soup was not sick." Johnson (1866) also declares that "persons who neither eat milk, butter, or beef have taken the disease and died from eating chickens that had it." Various other writers refer to the causation of the disease in man from eating the flesh of beef cattle, calves, hogs, or chickens as if the circumstance were well authenticated.

We have ourselves seen two cases of the disease in New Mexico in which inquiry did not bring to light any indication of milk or butter transmissions, while a possible origin was found in meat eaten at a Chinese restaurant. In a severe family outbreak occurring about a year before our visit, the trouble was attributed to meat. We are fortunately able to give a full description of the circumstances surrounding this outbreak in the words of the head of the family (A. M. H.), a man of unusual judgment and insight.

> About December 1, we butchered a calf that had had the run of the yard around the place. The weather turned warm and the meat began to spoil. My wife did not tell me about this, but tried to save as much of the meat as possible by trimming out carefully the tainted parts. We hardly ever use the liver and kidneys, but the girls had found some new recipes that they wanted to try and used both the liver and kidneys.
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> Our boy, the youngest child, was on a milk diet exclusively. He showed no signs of illness. One of my nieces ate very little meat at any time and had hardly touched the meat in question. She worked night and day for three weeks in caring for the rest of us without getting sick. The other niece had eaten some of this meat, and had a touch of the sickness. Our two little girls that died were always helped at table by me and no doubt got the same poison as I did. My wife also ate meat liberally.
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> Towards the last of November cattle came to my place for water. Many of them died afterwards from "alkali." A Mexican had his team around the place more or less; shortly afterwards one horse died from the same disease as the cattle. During this time it rained more or less and pools of water stood in many places in the yard, and I saw this calf drink from these pools several times, though it had access to good water. The calf had all the skim milk it wanted and was in fine condition.

Attention has already been drawn to the possible rôle of water in causing the disease in cattle. In man also there is some evidence of water transmission. McAnelly (1836) records several cases where the occurrence of the disease on a particular farm seemed to be connected with the use of a well water. The same writer adds, "The disease sometimes prevails in the human species in districts where the inferior animals are comparatively exempt and frequently where none of them are known to be affected at the time, as in the neighborhood of Johnstown, O., where the inhabitants use water from the wells while the stock get theirs from the brook before spoken of." Taylor (1842) also attributes a particular human case to drinking mineral water "at the very place most of our cattle and horses have died." Brewington (1876) makes the following interesting statements: "I do not believe that in this vicinity there is one in fifty persons that take the disease who gets it by using milk or butter from diseased animals. In places where the disease used to be most prevalent, the people used water from wells for cooking and drinking, but since they built cisterns and use water from them exclusively, they are entirely exempt from the disease."

Sager (1879) relates a specific case considered by him to be certainly caused by drinking-water: "April, 1878, was called to see McK.'s wife. He was a poor man, lived in a rented house, and no well water to use, consequently got their water to drink and for culinary purposes out of a ditch which contained clear water, but this ditch drained timbered land also. I found Mrs. McK. very sick with all the symptoms present peculiar to milksickness. Upon inquiry they informed me that they drank no milk, neither ate butter, as they had no cow and were too poor to buy the milk and butter. Neither did they eat any fresh meat. In both cases my conclusion was drawn in favor of the third proposition (water), being satisfied that heavy dashing rains will remove the germs from their fixed places and carry them into pools and ditches."

Pusey (1880) describes a series of cases very striking from the point of view of possible water infection: "It is claimed that all the patients got the disease on the Tate farm, which is situated half a mile northwest of the farm on which the Clarke family died. In July and August Tate's wife and two children died and three others recovered, all patients of Dr. Pennington of Benleyville. After the death of Tate's family the Clarkes bought his growing crop and the place was vacated till October; then the Clarkes went on the premises to dig the potatoes and to make sorghum. While engaged at this work four of them got sick so nearly together and so nearly alike and immediately after drinking of water that had stood overnight in a bucket near the cane pile, as to impress them with the idea that they had been poisoned by the water. Three of the Clarkes died and two recovered.

"About sixty years ago, as I learn by tradition, and within the memory of one person living in the vicinity, a family of the name of Hull, living on what is now the Tate farm, all died from milksickness. The water of two springs was believed to have contained the poison."

Conner (1904) mentions a case of supposed water transmission which, however, did not fall under his own personal observation.

In the limited number of cases of this disease that have come directly to our own knowledge we have not met with any that it seemed reasonable to ascribe to drinking water.

A few instances of supposed cutaneous infection are recorded. An anonymous physician writes from Indiana to the *Maryland Medical and Surgical Journal* (1839) as follows: "The late Professor John Eberle told me, when I visited him a year or two since, that he attended with Dr. Drake on two cases in Cincinnati, laboring under 'milk sick.' It appears that the men had driven a cow from Lafayette, in Indiana, to Cincinnati, where it died, and they determined to take off the animal's skin, being the only part of the animal which was available. One of them had cut his hand a day or two previous, and the other, in skinning, cut his finger with the knife, and four days after they were both seized with 'milk sick' and one of them died."

Sale (1871), apparently giving the results of his own experience, states that "in 1836 a cow died of the disease; two men skinned her and a woman rendered the tallow. They all died of the disease two days after." Other writers (see Elder, 1874) express the belief that one way in which the disease may be produced is "by skinning animals that have died of the malady." Hibbard (1844) on the other hand, is incredulous as to the disease having been contracted by skinning carcasses. In those localities where we have had the opportunity of studying this affection, no evidence of cutaneous infection has presented itself. Ranchmen and others have testified that they frequently opened the bodies of animals dying from trembles without experiencing any ill effects, nor have they known of any case of the disease in others contracted in this manner.

THE NATURE OF THE VIRUS.

a) **Behavior towards Heat.**—According to one observer (J. N. Smith, 1837) the active agent in or upon the soil is destroyed by heat: "About fifteen or twenty years ago, we are told that the disease was particularly severe in the edge of an adjoining county, and from some accident during a dry time in autumn the woods became ignited and burned over a circumference of several miles; and in the following autumn, either by accident or design the burning was repeated. Since which time there has never been a case of the disease in that neighborhood. And the inhabitants do not even think it necessary to keep up their cattle."

Yandell (1841) and Chesney (1880) mention that it was the custom to burn the carcasses of animals dead from trembles. C. H. Smith (1867) gives an interesting account of an outbreak observed by him: "All cases that occurred here were in American families, there not being one in a German family. Now the cows of the two classes run in the same ground and the cattle of both die with the disease; yet I have never known a case to occur among the Germans. The reason is, I think, plain. The Americans use the milk just as it comes from the cow, and the Germans boil what they drink."

Johnson (1874) is very emphatic concerning the action of heat in destroying the virus: "Heat also destroys the poison, whether in the milk, butter, or flesh, the opinion of Professor S. H. Dickson to the contrary notwithstanding. I have enquired of a great number of people living in various milk-sick regions as to whether cooked beef was ever known to impart the disease, and the invariable reply was, no."

Sager (1879) thus expresses his conviction: "What is the poison? . . . . We answer, fixed low organisms, and that fire destroys them. . . . . The above has been thoroughly tested by the farmers in the vicinity where I live. Mr. John Smith, Sr., and others have cleared pieces of ground with the timber standing of all the old logs and rubbish lying on the ground and consumed the same with fire. Since that, the same ground has been pastured with horses, cattle, and sheep with impunity."

One small family outbreak in Carlsbad, concerning which we have obtained first-hand information, affected two members of the family who drank raw milk; a third member who drank the same milk boiled escaped. Graff (1841) states that butter after being heated retains all its virulent properties, altho he also affirms that the extract obtained by boiling meat for several hours has no perceptible effect even when given in large quantities. Crawford (1908) has called attention to the discrepancy of Graff's statements.

b) Persistence in Soil, Hay, etc.—Under certain conditions the virus of milksickness may persist in the soil in a given locality for at least fifty or sixty years (Pusey, 1880) and probably for even longer periods. It is true, however, that as a rule such milksick tracts of land remain able to communicate the disease only if they are left in a wild or uncultivated condition. As long ago as 1822 Bennett wrote: "Those farmers who keep their cattle and horses in inclosed pastures which have been cultivated, do not lose them by this disease." The same opinion is exprest by Crook (1857), Simon (1888), and many others. Clearing, drainage, and cultivation of a milksick area destroys its dangerous quality. Pickard (1857) reports the following case: "Another family having suffered from its ravages, plowed up a pasture field, digged around the stumps, thoroughly turning all the soil, and sowed the field in grass, upon which they have kept their stock for 20 years, and at no time has milksickness made its appearance; while on other portions of the farm uncultivated, it is as fatal as ever." Drake (1841) in his elaborate memoir on Milksickness concludes that "clearing and cultivation, even girdling the trees, harrowing the ground, and sowing it with grass seed, destroys or renders inactive the cause, whatever it may be." In a letter received by us from Dr. Morrow B. Wilson of London, O., we are informed that farmers in that locality still find that drainage and cultivation of milksick areas destroy the virus in the soil; and cutting out the underbrush and letting in the sunlight is equally efficacious.

According to Gray (1877), Beach (1883), and others, the virus may be gathered and stored away in hay. Beach says: "That cattle *may* have trembles in the winter season, is a matter of occasional observation; and the old citizens generally attribute it to the feeding of cattle upon wild or swamp hay." The same author gives a specific case of trembles apparently due to hay cut from a meadow overflowed by drainage from a milksick locality. One writer (White, 1836) makes the following statement on the persistence of the virus in meat " . . . . one case occurred within our knowledge in the course of the last summer which was brought on by eating dried beef that had been slaughtered the preceding fall."

c) Effect of Season.—A difference in the seasonal incidence of the disease has been noted by many observers. Drake (1841) states that "it occasionally occurs in May and June, but its usual time of prevalence is August, September, October, and November." Dawson (1842), Shapard (1892), and many others refer to the more extensive prevalence of the disease in late summer and autumn than at other times of the year. Rawlings (1874) maintains that the "cause . . . . is affected by the change of season in the same way that malaria is." While in most localities an autumnal incidence is noticed, this is not invariable. Beck (1857) refers to its having prevailed in Kentucky exclusively in winter while in the locality from which he wrote (Cadiz, Ind.) it prevailed "in all seasons except winter." Beck adds, "If we have abundance of rain in the spring, with hot sunshine alternating with thunderstorms and growing showers, as we sometimes have the last of April and during May and June, then we confidently expect milk sickness in May and June. A dry spring and summer will postpone it till September or October." Dewey (1854) speaks of the disease as probably due to "a succulent plant" bearing a white blossom. According to this writer the plant in question is destroyed by the first hard frost "when it and the disease contemporaneously disappear." There is, however, abundant testimony that the disease occasionally appears in winter (Yandell, 1852; Beck, 1857; Waggoner, 1859; Beach, 1884; Shapard, 1892). In the Pecos Valley region the disease generally occurs in November and December, but we were told on reliable authority of some cases that occurred in March. We have seen human cases in Illinois in early July and in late November.

Altho there does not seem to be an exact and invariable correspondence between the season of the year and the disease, an autumnal incidence exists in most localities. This is one of the chief reasons for the frequent comparison of milksickness to malaria made by authors, and for the ascription of a "miasmatic" origin to the former malady. On the assumption that the virus of milksickness has its habitat in the soil, cattle might be supposed to contract the disease more readily at the season of the year when the pasturage is scanty and the herbage is consequently cropped closely. Many statements confirming this explanation might be cited in addition to those already quoted. One writer (Sager, 1879) makes the statement that sheep are more liable than other animals to contract trembles because of their habit of close cropping.

It seems to have been a common belief among farmers in certain milksick regions that cattle kept "up" till the dew had evaporated were less likely to develop the disease than if allowed to go out to pasturage in the morning early (Evans, 1860; Walker, 1886, *a*). An oft-quoted statement from Reagan (1884) also bears on this question: "It is known by all who live in the vicinity of the poison that the danger is when the dew is on vegetable matter, if it were vegetable in its origin it would poison at any time of the day, which is not the case. In order to test this matter they took hay from a settlement remote from this knob and let it lay out on the knob during the night and fed it to a healthy cow while the dew was on it. Again they tried the same and waited until the sun had thoroughly dried the hay, then fed it to a cow and it did her no harm." It seems possible to explain such observations as Reagan's by assuming that microorganisms present on the hay were killed by drying or sunlight. As regards the alleged influence of dew in favoring the production of disease it is evident that particles of soil (containing microorganisms ?) cling more readily to moist blades of grass than to dry herbage. Woodfin (1878) suggests that the influence of dew is only apparent and that the reason why cattle in some regions seem to contract the disease more readily if turned out to pasture early or brought home late is that they are able to range farther and so to reach the affected, and usually remote, tracts of land. Davis (1881) would explain the influence of dew by the fact that: "Animals eat more greedily when the vegetation is saturated with water then they do when the vegetation is dry."

One of the most remarkable features of this disease is its power of self-propagation. As already shown, the flesh of cattle dying from trembles will sometimes if eaten communicate the malady to other animals. If the accounts of numerous eyewitnesses are to be believed, the flesh of these animals in turn will give rise to fresh cases and so on with seemingly no limitation. Sale (1871), for example, records an outbreak in which the virus was passed from a cow to pigs and from the latter animals through the pork to man, while neither cow nor pigs showed any signs of illness. DeBruler (1858) relates an occurrence which fell under his own observation: A cow gave the disease to her calf which died and was eaten by two dogs; both dogs died with the usual symptoms of "tires;" a pet crow fed on the dogs' flesh also died. McCall (1830) cites one instance of the passage of the virus from sheep to hogs, and hogs to chickens. The chickens were used as food and caused milksickness in a man and wife and their children; one son "who ate none of the chicken or soup was not sick." Philips (1877), whose observations seem to have imprest him strongly with the infectious character of milksickness, declares with emphasis that the disease is "transmissible and reproduces its kind." Perhaps the most definite statement on this point is made by Graff (1841) who says: "This subtle poisonous principle, of whatever it may prove to consist, seems to possess the power of infinite reproduction, by some vital or chemico-vital action of the system of those animals poisoned by its influence. Thus, suppose one pound of flesh to prove sufficient to produce the death of another animal, it will be found that each pound of flesh of that animal so destroyed, will possess as active powers of destruction, and will, in its turn, serve to contaminate the whole body of another animal in the same degree. I had wished to repeat this so often as to demonstrate the possibility of its reproduction *ad infinitum*. In this I failed, from the difficulty experienced in compelling 'dog to eat dog.' From what I have observed, I would say that there exists a power of generation of the poisonous principle in the animal economy. This primary impulse being received from the specific action of some substance, vegetable or mineral, by some means obtained from the soil."

Our own observations and experiments upon the transmissibility of this disease will be considered more fully in another connection. It is sufficient to mention here that we have at various times fed several dogs (four) with the flesh of animals dead from trembles and have observed no ill effects. This corresponds with the irregularity in feeding experiments noticed by some other observers. Whatever be the cause, feeding does not act uniformly and constantly.

d) **Contributing Factors.**—One circumstance often remarked is the exemption of certain cattle in a stricken herd. On this point Coleman (1822) says: "Cattle and horses do not always become afflicted with the disease if allowed to range in the woods where the disease is common;" and similarly Woodfin (1878): ". . . . many animals may feed on the same lands and evidently partake about equally of the poison and some of them suffer violently and die; others suffer lightly and recover, and others still, perhaps the larger number, remain quite healthy; and that the same is true of families containing several persons." Gray (1879) mentions a family outbreak where the parents had the disease and a child subsisting on milk from the same cows showed "not the least symptom of the poison." Perhaps some of the differences observed are due to differences in the quantities of virus taken into the system, others doubtless depend upon variations in individual susceptibility.

There is no doubt that violent exercise is a predisposing factor and has much to do with the development of acute symptoms. "The people in the infected districts very often chase their beef cattle around with dogs until they are heated by the exercise; then if the cattle do not show any signs of the disease they are killed and eaten as beef without fear" (Davis, 1881). Dixon (1833) says: "It is one of the peculiarities of the disease that the poison occasionally lies long dormant in the system, and only becomes active when excited by some indiscretion or violent bodily exertion." Woodfin (1878) states that "beeves that have fattened in these infected localities, started to be driven to market, take the trembles and fail the first or second day, while other cattle feeding on the same grounds, left at home, remain healthy; and dogs eating the flesh of milk-sick cattle, by lying quietly during digestion, remain healthy, while others put on the chase, or otherwise overheated, soon sicken and die." Reagan (1884) asserts that, "It (the poison) lies quietly in the system for a long time without exhibiting any of its toxical powers until the person or beast is *forced to take exercise*." Another writer (Simpson, 1839) expresses his opinion that the causal agent may "exist and lie dormant" in the system for a day and finally pass off without harm "unless it is developed by some exciting agent." He also adds that the prominent exciting causes of the disease in man are "over-exercise and excess in drinking spirituous liquors." According to Logan (1849) a subacute form of the disease "may exist for months after the cause is once introduced unless removed by the sanative efforts of nature or by a proper course of remedial treatment, or it may be transformed into the acute form by long fatigue, fasting, or over-exertion and in some instances by neglecting the bowels or suffering them to remain constipated for some days." The practice of bleeding patients with this disease is said by Simpson to be highly injurious. Sale (1871) has reported the interesting observation that "when phlegmonous erysipelas attacked the face and scalp in the cases reported, all the grave symptoms, such as distress at the pit of the stomach, vomiting, constipation, etc., subsided."

e) **Elimination of Virus in Milk.**—The opinion has been exprest by several writers that when the virus of this disease is eliminated in the milk, the affected animal is in some measure favorably influenced by such elimination. It is even asserted that "cows giving milk never suffer from the disease, the poison being eliminated by the milk" (Johnson, 1874). Other writers express themselves in less sweeping terms: "Cows giving milk do not manifest strong and decided symptoms" (Jackson, 1881). On the other hand there are numerous instances reported where milch cows have died from the disease after their milk had been observed to give rise to the malady. Some of them have been cited elsewhere in this paper.

POSTMORTEM EXAMINATIONS.

There are few autopsy records giving any but the most meager details or bearing the stamp of any wide experience. The brief descriptions are for the most part couched in general terms. The stomach contents of cattle are said by one observer to be "dry" and he adds that "the liver has a morbid appearance" (Bennett, 1822). According to another, "In every case where animals who have died of this disease have been dissected, the heart and aorta have been found greatly enlarged and their inner coats sloughy" (Beck, 1822). Another says vaguely that the disease "is attended with gastric and hepatic lesions" (Miller, 1867). Rawlings (1874) states that the "liver has usually been found congested with blood of a dark color." Hibberd (1844) mentioned one condition which "obtained, I believe, in all the subjects that were examined, whether of the human or brute family, viz.: *a diminution of the caliber of the stomach and intestine.*" Davis (1881) mentions a case in which "the opposing internal surfaces of the small intestine at one place were united by adhesive inflammation for three or four inches of its length." Mendenhall (1861) also notes the evidence of change in the alimentary tract: "The stomach and intestine are inflamed; the mucous coat is measurably destroyed; the entire coats are in some cases gangrenous." Home (1843), who made several autopsies, states that the alimentary tract is always inflamed either as a whole or in part and that the mesentery likewise is inflamed, and the mesenteric glands enlarged. In one case "the liver was of a natural size, but looked very pale; its peritoneal lining presented in two or three places an inflammatory blush." Newman (1867) records the following unique observation: "In examining the animal (a milch cow) after death, the skin was found very much thickened and covered with small pustules." No other observer seems to have noted such a condition.

A few more detailed descriptions are scattered through the literature. Dickey (1852) describes a postmortem made 10 hours after death in which the peritoneum showed marked signs of inflammation. The small intestine also showed evidences of severe inflammatory action, particularly in the jejunum and ileum where "the mucous coat was easily separated by the finger nail." Peyer's patches were ulcerated, the spleen was enlarged, and "there was ramollissement of the substance of the liver." The kidneys were healthy. McClelland (1854) describes in somewhat similar terms an autopsy upon the body of a robust laborer made eight hours after death. This writer says that the liver was enlarged and softened, and that "evidence of inflammation existed through the entire course of the small intestine." Wayman (1841) says of a case examined 15 hours after death that there was not much emaciation, that the colon was dark brown with rose-colored patches, and that the liver was of a dark color and seemed unusually friable under pressure by the finger. He also states that the gall-bladder was much distended with a black pitchy bile, and that the spleen was much enlarged, of a deep brown color, and very soft. The peritoneum had reddish spots and there was some increased effusion into its cavity.

Preston (1843) describes an autopsy made 13 hours after death. The skin was brownish-yellow. The omentum major was in the first stage of inflammation; the liver was enlarged and the gall-bladder adherent to the ascending colon and distended with dark bile. The stomach and duodenum were inflamed, the jejunum and ileum "inflamed in various patches." Preston further describes the pancreas as being "twice as large as natural," the mesentery highly congested, the mesenteric glands enlarged, and the kidneys enlarged and softened. The lungs were said to be apparently pneumonic.

Carney (1847) reports a postmortem examination in the following words: ". . . . internal coat of the stomach, particularly the lower portion, gangrenous; whole intestinal canal exhibiting a highly inflammatory state; liver healthy except the small portion embracing the bilious, tar-black and hardened gall-bladder enlarged and filled with black unhealthy matter; stomach and bowels about empty; heart and spleen healthy."

Graff (1841) describes two autopsies made on dogs and one on a human subject. These are often quoted and have been made the basis of most of the statements upon the pathology of this disease that have found their way into textbooks and general treatises. Graff states that in one dog the intestines were much diminished in caliber and the stomach greatly contracted. The arachnoid was minutely injected and there were other evidences of cerebral inflammation. In another a similar condition of the stomach and small intestine was observed, the spleen was enlarged and the liver softened. "The lining membrane of the large intestine was nearly natural in appearance." Examination of the brain and cord showed marked evidences of meningeal inflammation. In an autopsy made upon a woman "by stealth at night, in the open air, and by the light of a single candle" Graff found likewise diminution in the caliber of the small intestine and stomach and profound inflammatory disturbances of the central nervous system.

The liver was said to have a peculiar appearance. These descriptions by Graff differ from those hitherto cited in their insistence upon severe inflammation of the brain and cord. Whether this is because Graff's cases were peculiar in this respect or simply because no examination was usually made of the central nervous system is uncertain.

Way (1893) in a brief note on morbid anatomy mentions having observed congestion of the abdominal viscera in "the lower animals" and in one case of a six-weeks-old calf intense congestion of the cerebral meninges.

Our own observations comprise examinations of several cattle, two lambs, one horse, and one human case.

a) **Cattle.** MACROSCOPIC.—All our observations on bodies of cattle dying from this disease were made in the vicinity of Carlsbad, N. M., in the autumn of 1907.

Externally the body presents nothing on inspection that is to be considered worthy of note. On reflecting the skin of the animal one can often detect an odor of acetone, particularly if the animal has just died. There are no subcutaneous lesions of any sort to be found.

On opening the cavities of the thorax or abdomen the odor of acetone is usually very marked.

The thoracic cavity.—Occasionally there may be a small quantity of clear yellow fluid present in the pleural cavities, which looks like serum and clots quickly on exposure to the air. There is no pleuritis. The *lungs* do not collapse greatly on opening the thorax. Several small areas of atelectasis may be found scattered over the dorsal aspect of the organs or at the apices of the upper lobes; at times one notices an occasional small area beneath the surface of the pleura which gives the impression that the part is filled with blood. The color of these organs varies at different times from a normal salmon color to a generalized purplish red, the latter condition being always found after a relatively long period of illness. The lungs feel boggy and on section exude a great deal of frothy fluid, i. e., they are in an edematous state, and this circumstance accounts for the incomplete collapse of the organs on opening the thorax. Sections of the most edematous portions, however, float in water. We did not on any occasion find any traces of bronchopneumonia or lobar pneumonia. The mucosa of the trachea and bronchi showed no signs of inflammation. No ecchymoses were found on the pleural surfaces.

The heart.—As a rule the pericardial sac contained varying quantities of clear straw-yellow fluid (50 to 175 c.c.) which clotted on exposure to the air. Pericarditis was not met with, at least such as could be laid to the disease; in one instance the visceral pericardium was thicker than normal, giving a uniform grayish tone of color to the whole of the organ—this was evidently due to some old attack of pericarditis. The right heart was generally found distended with blood, whereas the left side of the organ was usually found empty. Among the most noticeable things seen on opening up the pericardial sac were numerous areas of ecchymoses beneath the visceral pericardium, distributed chiefly along the course of the cardiac veins from base to apex and at times numerous at the base of the heart around the roots of the great vessels. These areas varied in size from that of a mere pin-point to irregular areas measuring approximately 2 by 2.5 mm. and the accumulation of blood sometimes bulged the serous covering up above the surface about 1 mm. in places. In some of the animals ecchymoses were of slight extent and in one case absent. No ecchymoses were ever seen on the parietal surface of the pericardium. As a rule the heart muscle was always definitely paler than normal, sometimes giving the impression of the existence of cloudy swelling, and at other times showing small areas of fatty metamorphosis. On opening the heart there were never present any evidences of the existence of endocarditis. In two cases ecchymoses were found beneath the endocardium over the tricuspid valves close to their bases, the accumulation of blood bulging up the endocardium about a millimeter high. On section the musculature showed the same appearances as seen on the outside, namely, either fatty areas or streaks, or more or less generally cloudy swelling; this was brought out particularly on making sections of the muscle in the left ventricle, the apparent fatty areas being well marked.

The abdominal cavity.—On opening the peritoneal cavity there was in general little or no fluid present above what might be considered normal. No evidences of peritonitis were ever seen. In some cases small scattered areas of ecchymoses were found beneath the parietal peritoneum; these never measured over three square millimeters; more rarely were such found beneath the visceral peritoneal coat. The stomachs were usually well filled with food material in contradistinction to the intestines, both small and large, which were usually empty. The appearance of the small intestines, particularly in the duodenal and jejunal portions and less so as the large gut was approached, was that of a general and deep injection of the vessels beneath the peritoneal wall and within the walls of the gut itself. The large gut, as a rule, was in an apparently normal state and occasionally contained some fecal material.

Liver.—The most conspicuous condition pathologically among the organs was the state of the liver. Uniformly this organ was much enlarged, of a purple red color, being full of blood, with at times areas or streaks showing yellowish against the red color of the rest of the viscus. The gall-bladder was most often full of bile of a dark green color. On removing the liver from the body and applying pressure to it, the dark red color disappeared and was replaced by that of a reddish yellow. The consistency of the liver substance was much diminished and it required little pressure of the fingers to produce rupture. At times an occasional ecchymotic spot could be seen under the capsule. On section the organ dript considerable blood and exposed a reddish yellow surface, the presence of the blood vessels everywhere being plainly marked out, giving the typical appearance of the "nutmeg" liver. The parenchyma was markedly fatty. The gall-bladder in some of the animals on being opened showed a small degree of injection of its mucous coat; at other times it looked quite normal. The bile was always clear and of a dark greenish color.

Spleen.—The spleen, so far as determined, was little, if any, enlarged in any of the cases, the capsule often being wrinkled up and thick and of a pearly gray color. In two of the animals the spleen showed several small subperitoneal ecchymotic patches, but as a rule these were absent. On section the organ was of a deep maroon red color, and the Malpighian bodies were not seen at all distinctly, sometimes not at all. The fibrous tissue framework was in all cases very evident. The consistency of the spleen was thought to be normal in all cases, at least it was not particularly soft.

Kidneys.—The kidneys, so far as we were able to judge, were always enlarged and engorged with blood, having in consequence a deep brown-red color. In certain of the animals the kidneys showed a definite cloudy swelling of the parenchyma, and in one instance slight fatty change. On section the organs contained a very considerable quantity of blood. The Malpighian tufts always stood out plainly on the cut surface. On the elimination of the blood from the organs in certain of the cases the appearance of cloudy swelling or of fatty metamorphosis seen in the organ before removal from the body vanished so that it could not be determined with certainty whether there existed any degenerative changes or not.

Bladder.—The bladder often appeared on the outside deeply injected, but this condition was not constant. On opening the viscus the mucous surface was at times found to be injected, at times not. There were no ecchymoses seen under the mucosa. In certain of the cases the urine contained within was cloudy and apparently contained traces of blood. The adrenals seemed to be normal.

Intestines.—On opening the small intestines they were seen to be much injected in the mucous membrane and also showed here and there in some of the animals small ecchymoses in the mucosa. As a rule the gut in the duodenal portion held a considerable quantity of greenish yellow mucus mixt in small amount with material from the stomach. Passing downward through the jejunum and upper parts of the ileum, the mucus in the gut was of a very tenacious character and of a definite yellow color, with little or no food material in it; it clung to the walls of the gut strongly and was mixt with small bubbles of gas. The large gut on being opened appeared normal in all the animals.

Muscles.—The general musculature of the animals was normal in appearance, being not pale or of deeper tint than usual; no ecchymotic spots were ever found beneath the muscle sheaths or in the muscle substance.

Brain.—In only one animal was the brain exposed, and this only with difficulty on account of lack of proper tools. In this case there was some congestion of the meningeal vessels, but no redness of the parenchyma of the brain. On section the ventricles of the brain appeared also congested and there was an excess of fluid, which was not, however, cloudy or blood-stained.

MICROSCOPIC. **P. B.**—Three-year-old Hereford bull, shot in head with rifle while in an early stage of the disease (Fig. 1). Tissues preserved in formalin; stained with hematoxylin and eosin.

Heart.—Left ventricle: Muscle fibers have for the most part lost their striations, are fibrillated, nuclei frequently swollen, vesicular, and do not stain well.

Lung.—Hyperemia; some atelectasis; some alveoli are filled with serum, others with red blood cells. No bronchitis; no bronchopneumonia.

Liver.—Hyperemic; cloudy swelling in moderate degree, affecting the liver cells here and there in the columns; slight amount of fatty change in some parts of the section.

Kidney.—Hyperemia; glomerulitis present as shown by the swollen cells of the capillary loops and the apparent increase of nuclei, and much coagulated material in Bowman's capsule. Parenchymatous degeneration of a mild degree present in the convoluted tubes more particularly; much granular material within the lumina of many of the tubules.

Spleen.—Hyperemic only.

Duodenum.—Much round-cell infiltration of the mucosa and hyperemia; epithelium everywhere intact.

P. H. 1.—Two-year-old heifer—pregnant; autopsy five hours after death. Formalin preservation; hematoxylin and eosin.

Heart.—Left ventricle: A moderate degree of parenchymatous myocarditis present; striation cannot be discerned, many nuclei pale and distorted and absent; muscular substance in places granular. On cross-section, fat droplets can be seen within the cells.

Lung.—Hyperemia; atelectasis in certain portions; in others edema which affects some of the smaller bronchioles as well as the alveoli, some local emphysema. No bronchitis or bronchopneumonia.

Kidney.—Hyperemia; a mild grade of parenchymatous degeneration of the convoluted tubules and of the glomeruli.

Spleen.—Hyperemia; altered blood pigment in some cells of the pulp; otherwise normal.

Adrenal gland.—Hyperemia.

Pancreas.—Hyperemia.

Liver.—Hyperemia. Parenchymatous cells swollen and filled with large and small droplets of fat; some few nuclei degenerating. No cholangitis; bile ducts flattened out with the pressure of the swollen liver cells.

Stomach.—Fourth division (three sections): All normal. Fourth division (pyloric end): With the exception of two small foci of round-cell infiltration in the deeper part of the mucosa, the specimen is normal.

Small intestine.—Acute enteritis: loss of columnar epithelium from the villi; invasion of the mucosa by round cells; enlargement of the solitary follicles with occasional necrotic areas within the follicles; in one of the follicles resting on the inner muscular coat of the bowel is a partial section of a possible vermicular parasite in a coiled attitude, and having an apparent chitinous covering; it lies in a smooth-walled cavity. Edema of the submucosa and general hyperemia.

Fetus (about four to five months old).—Formalin; hematoxylin and eosin.

Liver.—Cloudy swelling of the liver cells is the prominent feature of the specimen; in many cells, however, the nuclei stain pretty well altho the protoplasm barely stains at all; some of the cells contain fat droplets. The capillaries are filled with blood and show a high degree of round-cell accumulation in which the sizes of the individual cells differ considerably, and in many areas they are found massed together; in the blood also can be found a relatively large number of large, round, polynuclear cells which take a deep chromatin stain and whose protoplasm stains well with eosin (Engel's metrocytes ?). Bile ducts are seen in many places.

P. H. 2.—Young heifer, 10 hours after death. Formalin preservation, stained in hematoxylin and eosin.

Heart.—Left ventricle: Parenchymatous degeneration, fatty metamorphosis in certain bundles of fibers; much finely granular brownish pigment noted in the muscle cells in some places.

Cortex Cerebri and Cerebellum.—Appear normal.

Lung.—Generalized edema, with a few scattered alveoli air-containing. Occasional areas of atelectasis. Interlobular tissue edematous. Hyperemia. No bronchitis or bronchopneumonia; no pleuritis.

Kidney.—Acute diffuse glomerulonephritis; in certain of the collecting tubules are seen some polymorphonuclear leukocytes. In two localities of the section are areas of acute interstitial nephritis.

Spleen.—Hyperemic, otherwise normal.

Liver.—Generalized cloudy swelling accompanied by a moderately high grade of a fatty metamorphosis, the fat occurring in small and large droplets. The parenchymatous degeneration is most marked in the middle and inner zones. Pressure of the swollen cells partially obliterates the capillaries and smaller bile ducts, altho the central veins are well filled and prominent.

Adrenal gland.—Hyperemic, but otherwise quite normal.

P. H. 3.—Young heifer, moribund, killed by blow on head, autopsy at once. Formalin preservation; hematoxylin and eosin.

Heart.—Left ventricle: Slight evidences of cloudy swelling in some of the muscle bundles accompanied with fatty changes. Striation is indistinctly present in a few places.

Lung.—Hyperemia; some atelectasis; no inflammatory reaction anywhere; no edema. Another section: Hyperemic; considerable atelectasis, and in these areas there appears to be some multiplication of connective-tissue elements. The walls of the alveoli are everywhere thickened by increase of their connective-tissue cells. No inflammatory reaction of bronchi, or of neighboring tissue, or of interlobar septal tissue.

Kidney.—Moderate degree of diffuse glomerulonephritis; some of the tubules hold granular material and a few red blood cells.

Adrenal gland.—Normal.

Pancreas.—Normal.

Spleen.—Practically normal, there being some dark brownish pigment scattered about throughout the specimen.

Liver.—Nearly all lobules show cloudy swelling distributed in the middle and inner zones accompanied by fatty changes. Capillaries are indistinct in many places, due to the pressure of the enlarged liver cells; central veins full of blood. No cholangitis.

Stomach.—First division (two sections). Normal.

Small intestine.—Enteritis, small-cell infiltration, loss of columnar epithelium and in some places partial destruction of the Lieberkühn's follicles. Hyperemia.

Calf 1 (Galton's).—Fell suddenly dead while being chased. Formalin; hematoxylin and eosin.

Liver.—Cloudy swelling accompanied by a high grade of fatty metamorphosis; capillaries and smaller bile ducts comprest by the enlarged liver cells. Central veins widely open and filled with blood.

b) Lambs.[1]—The two lambs previously mentioned were chloroformed while in a moribund condition and their bodies examined immediately. The following notes were made:

Lamb 1. SECTION.—On reflection of the skin there was no sweetish odor noticed. Superficial blood vessels were not injected. Inguinal and axillary glands were not found enlarged. Abdominal cavity: There was no peritonitis and no excess of fluid found. The stomach was very full; small intestine empty and of a deep red color; the large intestine contained a few fecal masses and appeared normal. The omentum was in a normal state. The mesentery was studded with small hemorrhagic areas or ecchymoses, measuring 1–3 mm. in diameter; there were a few small hard thrombi found in the mesenteric veins. The mesenteric glands were not enlarged. The liver was of a very dark red color and filled with blood; the under surface showed a normal appearance, except the quadrate lobe which showed a marginal hemorrhagic area 2×8 mm.; the diaphragmatic surface of the organ presented on its left lobe four small whitish patches about 1 mm. in diameter not elevated above the surface, and looking somewhat like scar tissue. On pressing the liver the blood could be locally driven out and the tissue took on a decidedly yellow appearance, and was very friable, the changes could be described as fatty metamorphosis. The gall-bladder was very full but showed no inflammation. The spleen was of a bluish white color and hard to the touch; on section the Malpighian bodies could not be made out. The kidneys were both apparently normal; the adrenal glands were likewise. The retroperitoneal glands were not enlarged. The urinary bladder was full and the vessels were injected. On opening the small intestine its contents were of a frothy yellowish mucous character; no nodules or other peculiarities were noticed. The stomach was filled with grass and the mucous membrane of the four portions was seemingly in a normal condition.

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[1] The naked-eye observations upon the bodies of these animals were made by Mr. D. D. Todd, Fellow in Bacteriology.

Thoracic cavity.—The lungs were collapsed, of decidedly reddish color, and showing many hemorrhagic areas measuring from 1 mm. to 2 cm. in width; these were most commonly present at the roots of the lungs. Apart from the presence of scars on the pericardially opposed surfaces of both organs and the occurrence of the hemorrhagic areas the organs were in a relativly normal condition. The heart appeared normal. Pericardial sac and membranes in a normal state. Blood in the heart was markedly laky.

Brain and meninges.—Brain matter was very soft. In the posterior part of the superior longitudinal sinus was found a small thrombus. Meninges normal and there was no excess of fluid beneath them.

Lamb 2.—Female, age 10 weeks. This animal in contradistinction to the first often struggled to get on its feet but was unable to rise, and after such struggles it kept its feet and legs going in a walking motion for some seconds. Breathing was forced and jerky but regular at the rate of 33 per minute. Pulse 111 per minute.

SECTION.—No palpable glands observed beneath the skin. No odor of a sweetish nature on reflecting the skin.

Abdominal cavity.—Considerable peritoneal fluid present altho there was no peritonitis present. The small intestine was in greater part injected deeply; a few isolated areas 15–30 cm. appeared normal; these latter areas felt thicker to the touch than did the injected areas. No nodules were found on the external surfaces. The mesentery contained numerous hemorrhagic spots as did that of Lamb 1. The venous system of the mesentery was full. The mesenteric lymph glands were much enlarged and elongated. The large intestine was injected, contained very little fecal matter, and was filled with gas. The liver was soft, friable, filled with blood which on being pressed out in parts showed a yellowish color to the tissue; fatty changes were manifest; there were several hemorrhagic areas found on the under surface of the liver. The spleen was bluish-white in color, hard, and bound down to the diaphragm by numerous fibers; on section the structure of the organ could not be made out. The kidneys showed no abnormality. The adrenal glands were injected and swollen. On opening the small intestine it was found to contain a yellowish mucous material with a sweetish odor. Erosion of the mucosa was noticed to be limited to those areas that were deeply injected; no nodules seen in the mucosa anywhere.

Thoracic cavity.—There was present a slight excess of pleural fluid, altho there was no pleuritis noticeable. Left lung collapsed; color reddish, with numerous hemorrhagic areas scattered over its surface; the right lung was not collapsed, was of a clay color, and showed many hemorrhagic areas at the root.

Heart.—There was no pericarditis present nor hemorrhages; a slight amount of cloudy fluid was present. Heart muscle appeared normal; blood within the organ was laky. There were no lesions of the valves.

MICROSCOPIC. **Lamb 1.**—Alcohol preservation; hematoxylin and eosin.

Heart.—Certain of the fiber bundles show parenchymatous degeneration together with some fatty changes.

Lung.—With the exception of a few scattered air cells the tissue is normal.

Kidney.—Tissue not well preserved, appearances doubtful; perhaps there had been parenchymatous degeneration.

Small intestine.—Normal.

Liver.—Parenchymatous degeneration with fatty changes is seen throughout the whole specimen, but of a mild order, and chiefly confined to the outer and middle zones of the lobules. No hyperemia.

Lymph gland.—Apparently normal.

Lamb 2.—Alcohol; hematoxylin and eosin.

Heart.—Normal.

Lung.—Hyperemia; two small areas of polymorphonuclear leukocytic infiltration in the immediate vicinity of two bronchioles; other places normal.

Kidney.—Acute diffuse glomerulonephritis; some fatty changes found in some of the tubules. No interstitial changes.

Liver.—The section shows a generalized cloudy swelling of a moderate degree, occasionally some of the lobules are more severely affected than are others. In one or two places there are accumulations of small round cells at focal points. The blood capillaries and smaller bile ducts are much compress; central veins widely distended with blood. No cholangitis.

Lymph gland.—Appears normal.

Spleen.—Compared with the human spleen there is more connective tissue distributed throughout it than normal; otherwise there is nothing abnormal.

Intestines.—Small. Not sufficiently well-preserved for description. Large. Hyperemic only.

Adrenal gland.—Normal.

Spinal cord.—Too poorly preserved for description.

c) **Horse.** Just outside of Carlsbad an opportunity occurred of making an examination of the carcase of a horse said to have died of "alkali." As the animal had been dead for at least 15 hours and left exposed to a hot sun the body had been so invaded by *B. welchii* that the tissues were everywhere so heavily stained by laked blood that it was impossible to make any interpretations of a satisfactory nature.

However, near Otis, N. M., we had a chance to make an autopsy on a horse one hour after death, and in general the conditions found were closely similar to those seen in cattle.

MACROSCOPIC.—*Pericardium* contained a large quantity of clear, straw-colored fluid. There were no evidences of inflammatory reaction seen, and no ecchymotic spots. *Heart* exhibited beneath the epicardium of the right ventricle, around the base of the organ, and along the course of the coronary vessels a large number of ecchymoses of small but variable size. The myocardium, particularly of the right ventricle, looked paler than normal; and on section small scattered areas of probable fatty change were seen. No valvular lesions existed.

Lungs.—The only appearances of note were great hyperemia and edema in all portions of the organs. There were no signs of inflammation to be noted anywhere.

Liver.—Enlarged (?), purplish red in color; capsule smooth, thin, and free of ecchymoses; friable; on section the lobules could not be made out on account of cloudy swelling.

Spleen.—Capsule thick, grayish in color, wrinkled, and exhibiting a few small ecchymotic spots. On section, the color was a chocolate red; soft; and the Malpighian bodies invisible. The organ was not seemingly enlarged.

Kidneys.—The kidneys appeared to show cloudy swelling, but as they contained much blood this was not readily and certainly established.

Intestines.—In the small intestines there were found at irregular intervals nodules lying in some instances close below the peritoneal surface and in others somewhat more deeply imbedded in the wall of the gut. Viewed from the outside they measured in diameter about 4 or 5 mm. and were elevated above the surface in some cases full 2 mm., in others they projected about 1 mm. Those in certain instances were of a gray-yellow color surrounded by a zone of injected vessels and one or two of the nodules showed some traces of localized peritonitis capping, as it were, the apex of the nodule. In all there were eight of these nodules. On opening the gut it was found that these nodules had their origin in an inflammation of some solitary lymph nodes situated deep in the mucosa. In one part of the small intestine close to a nodule was seen imbedded fairly firmly a piece of hard foreign matter, which was supposed to be a thorn that had been swallowed and had penetrated the intestinal wall; this was later on found by microscopic examination to be the necrotic core of one of the nodules that evidently had ruptured through into the lumen of the gut.

Some small and large patches of ecchymoses were found in the mucous membrane of the duodenum, jejeunum, and ileum. The contents of the tract as a whole were largely made up of a greenish yellow, tenacious mucus. The colon appeared to be normal. The peritoneal surface of the abdominal cavity presented a few ecchymotic spots. There was a very definite odor of acetone on opening up the cavities.

MICROSCOPIC.—Formalin preservation; hematoxylin and eosin.

Heart.—Left ventricle: Altho striation can be generally discerned, the muscle fibers in many places are finely granulated, nuclei absent or very vesicular and staining poorly.

Kidney.—Some glomerulitis present. Acute parenchymatous nephritis of high degree present nearly everywhere. Hyperemia.

Liver.—More or less generalized parenchymatous degeneration throughout the preparation, affecting most intensely the middle and inner zones of the lobules, with accompanying fatty changes confined largely to the middle zone. Pigment of a brownish color is to be noted in the columns of cells in the more intensely degenerated zones. Considerable hyperemia exists throughout the section. No cholangitis.

Intestines.—*a*) Duodenum: Marked inflammation of the mucosa and submucosa as shown by the hyperemia, great round-cell infiltration, loss of columnar epithelium on the villi, and the swollen or atrophic conditions of the latter in several situations.

b) Jejunum: Conditions are somewhat similar to those in the duodenum only of a much less severe degree.

c) Ileum (section through a node in the wall of the gut): The preparation shows that the whole of the tissue is in a state of acute inflammation, there being intense cellular invasion by round cells, polynuclear and large wandering cells, accompanied by marked edema from mucosa to peritoneum and hyperemia. The epithelium is lost from the major portions of the villi, and in one locality an ulcerative process has been in progress so that there has resulted a considerable loss of the several structures constituting the mucosa, so that there remains only a thin layer of mucosa above the muscularis mucosae but entirely devoid of any suggestion of epithelial structure. This zone of denudation is seen to be surrounding a conical mass of necrotic tissue whose base lies free toward the lumen of the gut, its tapering apical part passes outward through all structures of the intestinal wall until it rests upon the inner surface of the inner muscular coat of the bowel. Throughout its course this necrotic mass is sharply demarcated and partially loosened from the surrounding inflamed tissue. So far as can be ascertained its origin cannot be traced to a thrombosed artery as suggested by the shape of the mass. The subperitoneal tissue is very edematous and filled with various types of inflammatory cells, and altho in places the cells of the peritoneum itself are missing, it is in all likelihood due to rough handling of the preparation, as there is no coagulated lymph anywhere to be seen in the denuded areas.

d) Human Case. AUTOPSY.—We have seen but one fatal human case. This was one of the Morris cases elsewhere referred to (p. 416). Death occurred at 12 noon, November 26; the autopsy was begun at seven o'clock the same evening. (Oil light.)

H. J., 8 years.—The body is that of a white female child, 52 inches in length, and about 65 lbs. in weight; fairly well nourished. Trunk not yet cold.

Livor mortis discerned on left side of face and over all dependent parts. Rigor mortis of lower limbs; upper supple (undertaker present stated that the arms were also rigid, but had been broken down by him).

Mucous discharge from right nostril (stomach contents?); fecal discharge of a watery nature from the anus. Strong odor of acetone from the body.

On reflection of the skin the subcutaneous fat was found to be rather scant in amount. Pectoral muscles were dark red in color. The acetone odor was quite marked over the area denuded of integument.

Abdominal cavity.—Peritoneal cavity shows no excess of fluid and no signs of peritonitis; no ecchymoses visible; omental fat scant. The liver does not project below the costal margin; it is, however, apparently very fatty. The intestines (ileum) are empty and of a generalized pinkish color; the colon is filled with fluid contents and bluish-gray in tint. The stomach is partially filled with fluid; it is of a normal color tint. Pancreas firm and of a pale pinkish color. The spleen is not visible as the intestines lie undisturbed.

Individual examination of the abdominal organs. The small intestine.—The duodenum appears from the outside to be injected and this injection passes down for a short distance over the jejunum and then the rest of the gut is generally of a pink color. The mucosa of the duodenum was generally injected and somewhat edematous. On opening the jejunum it is found to contain a slight quantity of a tenacious yellowish mucus and the mucosa is of a definite pinkish tint everywhere; there does not seem to be any edema or inflammation, and there are no erosions of the mucosa. In the lower portion of the small intestine, the ileum, there can be seen before the gut is opened several dark purplish spots; these are found to correspond to the lymphoid plaques, Peyer's patches; in the opened gut they are found to be in a state of very moderate hyperplasia and are of a rather purplish-red color; in no instance do they show any signs of erosion, nor anywhere stand markedly above the general surface of the mucous membrane.

The colon.—The contents of this portion of the tract are brownish, watery, and have a fecal odor. In the descending portion there can be seen three or four small areas of congested vessels, otherwise the gut is pale in color. When washed free of contents and critically examined there is seen to be general folliculitis of mild degree; even when examined with a hand lens there cannot be discerned any process of erosion, simply hyperplasia.

Stomach.—Contents brownish watery; mucosa covered with sticky mucus; no rugae visible; seemingly normal.

The mesenteric glands are everywhere moderately enlarged and, on the whole, firm to the touch.

The liver.—The organ is of a markedly yellow color; not enlarged; capsule smooth and showing no ecchymoses; it is firm to the touch and is not friable. The gall-bladder is not distended and contains a dark brownish-green bile which is rather watery in consistence. On section, the general architecture of the organ can be made out without difficulty; the central parts of the lobules are brown in color while the peripheries are very distinctly yellow. No necroses of a focal nature were discoverable. The bile ducts and canals were nowhere distended.

The kidneys.—Both looked alike, if anything a trifle smaller than normal. In color they were of a yellowish-pink cast. Capsules everywhere smooth and non-adherent. No infarcts seen. On section, the cut surfaces had a very definite yellowish color, evidently fatty; the cortex was somewhat greater than the normal in depth; the interlobular vessels were readily discernible, but not so the Malpighian tufts (probably on account of the kerosene light); the pyramids were also of a fatty appearance. The pelves of the organs appeared normal. No chronic interstitial nephritis.

The adrenal glands.—Both seemed to be normal.

The spleen.—This organ did not appear to be enlarged. It was firm as is the normal. Color, a normal brown-red. Capsule not thickened. On section, the spleen did not contain any excess of blood; no interstitial splenitis; the Malpighian bodies stood out plainly; there were no infarcts found.

The urinary bladder.—It contained about 50 c.c. of a clear pale yellow urine (preserved). There were no signs of cystitis. The ureters appeared normal.

Uterus and ovaries.—The sex organs appeared normal.

Pancreas.—It seemed normal.

Thorax.—The pectoral and intercostal muscles were of a dark red color. On removal of the sternum the thymus gland was seen to be of a diamond shape measuring $1 \times 1\frac{3}{4}$ inches $\times \frac{1}{4}$ inch deep; it was soft to the feel of the fingers and did not appear to be abnormal in any respect. The precordial space measured about $2\frac{1}{2} \times 2\frac{1}{2} \times 3\frac{1}{2}$ inches.

Pericardium and heart.—The pericardial sac on being opened was seen to contain about 15 c.c. of a clear yellow fluid (some put in a sterile tube). There were no ecchymoses on the parietal walls. No signs of pericarditis. The heart did not seem to be enlarged; the cavities of the right side were filled with blood, while the left chambers appeared to be empty. Beneath the visceral pericardium at the base of the heart and at the roots of the pulmonary artery and aorta were seen a number of very small ecchymotic spots not measuring more than 1–2 mm. in diameter; a few were also found alongside the veins of the anterior interventricular groove; these were quite minute. On opening the heart the right auricle and likewise the right ventricle were found to be filled with postmortem clots; the foramen ovale was closed and the endocardium appeared to be normal. The right ventricle: The tricuspid valves were found in a normal state, as also the pulmonary-artery valves; the endocardium everywhere was smooth and showed no ecchymoses. The left side: There was nothing found of an abnormal nature in the left auricle or in the left ventricle. The heart muscle generally seemed to be of normal consistence and on section appeared to be of a good color and gave no evidence of myocardial changes.

The lungs.—These organs did not collapse greatly on the opening of the thorax. The pleural surfaces were everywhere smooth and showed no visible signs of inflammation. There was no excess of fluid.

The *left* lung was voluminous; along the free edges the upper lobe was a little emphysematous and pale red in color; elsewhere the organ was of a dark red color, crepitant, but boggy. On section, the upper lobe gave evidence of chronic passive congestion, while the lower lobe was very edematous, considerable quantities of frothy fluid being set free on pressure; the bronchi did not appear to be inflamed.

In the *right* lung, as in the left, the upper and the middle lobes showed evidences of chronic passive congestion; the lower lobe in greater part was of so dark red a color and so airless as to look like liver; it was hepatized, but in small portions toward the anterior it contained some air and was crepitant. The bronchi in the middle and the lower lobes in some places were in a state of inflammation and pus oozed out of them on being cut across.

Brain and meninges.—The calvarium was removed and the meninges and the brain examined carefully; so far as could be seen there were present no abnormalities. Veins on cortex somewhat turgescent.

MICROSCOPIC. **H. J.,** Morris, Ill.—Tissues in formalin; hematoxylin and eosin.

Heart.—Right ventricle: In cross-section of a part of the specimen there are found not a few fibers that contain fat droplets, centrally disposed. In longitudinal section, loss of striation is the only feature to be noted departing from the normal. Left ventricle: In cross-section one can detect areas in which are the cut ends of certain bundles broken up in granular fashion; nuclei are less abundant, and fat droplets can be detected here and there. In longitudinal section no bundles appear in the preparation suggestive of myocardial change; striation and other conditions of the muscle cells appear to be normal. There is, however, a definite degree of interstitial inflammation manifested in the increase in number of the nuclei of the connective tissue lying between the muscle bundles together with some round- and polynuclear-cell invasion.

Cerebrum and cerebellum.—Apparently normal. Vessels of the pia-arachnoid hyperemic.

Lung.—Much hyperemia; air-containing alveoli numerous, but in other places there is edema or atelectasis. No signs of any kind of inflammatory reaction.

Kidney.—Acute diffuse parenchymatous nephritis and glomerulitis. In company with the parenchymatous changes there is a high grade of fatty metamorphosis in many of the tubules, the fat being laid down in the shape of fine droplets.

Liver.—The cells of the parenchyma present a high degree of fatty degeneration everywhere, the cells being loaded down with small and large fat droplets. The nuclei of the cells are often absent or stain poorly. The blood channels are very hard to see on account of the generally swollen condition of the parenchymal cells, while the smaller bile ducts are comprest and the central veins widely open and filled with blood. There is one minute focal point of round-cell invasion, not accompanied by any signs of necrosis. No focal necrosis; no cholangitis.

Intestines.—All specimens show lack of sufficient penetration of the preservative to allow of any trustworthy interpretation of appearances. If one may judge from what is presented hyperemia only prevails.

Thymus gland.—Apparently normal.

Small intestine.—Zenker preservation; hematoxylin and eosin. Section through a Peyer's patch. There are the usual signs of inflammatory reaction in the close neighborhood of and in the lymphatic tissue of the patch, there being loss of columnar epithelium, cellular invasion of the villi, and engorgement of the veins. The Peyer's patch shows inflammatory hyperplasia but no necrosis of its substance anywhere.

In addition to this case we have obtained through the courtesy of physicians material from two other human cases.

Dr. Goldsmith's Case.—This was material from one of the fatal cases in New Mexico mentioned on p. 416 (M. H.). It was kindly given to us by Dr. A. A. Goldsmith, of Chicago, to whom it had been sent for examination in January, 1907. Formalin preservation; hematoxylin and eosin.

Lung.—Considerable general hyperemia. Many alveoli edematous and in places the red cells have escaped as well into the alveoli. There are no evidences of bronchitis, bronchopneumonia, or pneumonia.

Kidney.—Intense diffuse parenchymatous and glomerular nephritis. Some necrosis and much fatty degeneration of the convoluted tubules, as well as fatty changes in the descending loops of Henle and of the collecting tubules. The tissue was probably hyperemic, has been affected by its prolonged stay in the formalin so that the blood cells are not particularly well preserved.

Liver.—If the bile ducts and the blood vessels of Glisson's capsule could not be made out, the section would be doubtless taken for adipose tissue, so intense is the fatty degeneration present. The nuclei of the liver cells can be made out only here and there.

Spleen.—Some evidence of postmortem change throughout the specimen. In all likelihood the organ was considerably hyperemic, the size of the Malpighian bodies being encroached upon. There might have been some swelling of the cells of the reticulum together with some increase. No increase in the connective tissue apparent.

Dr. Maple's Case.—This case occurred in Shelburne, Ind., in the fall of 1906, and we are indebted to Dr. James B. Maple, of Shelburne, and to Dr. B. V. Caffee and Dr. Millard Knowlton, of Terre Haute, for information concerning it. The autopsy was made by Dr. Maple who has kindly furnished us the following notes:

Boy, James, age 16 years; previous health good; mother died a few days earlier of the same disease. Had been sick three weeks and was suffering from relapse when seen; sweetish breath, frequent and severe vomiting, bowels had not moved for 15 days, temperature was subnormal until day of death when it rose to 102°. Autopsy findings: *Thoracic cavity:* Lungs edematous, heart negative. *Abdominal cavity:* Not distended, no peritonitis, visceral peritoneum injected. *Stomach:* Contained nothing except about a pint of castor oil mixt with a greenish fluid; contents had a sweetish smell, like that of the breath; the mucosa of the stomach was highly inflamed and contained one ulcer with another area which was just ready to ulcerate; there was evidently an intense gastritis. *Intestines:* Both large and small were distended to their usual size with gas; on slitting them from one end to the other less than a gill of contents was found; there were constrictures every few inches in the course of the small gut, but there did not seem to be any scar tissue at these places. *Mesenteric lymph nodes:* Were enlarged and seemed to be inflamed. *Liver:* Was much enlarged, yellowish-red, and hard "as if it were stuffed with fat." *Pancreas:* Size normal. *Spleen:* Seemed normal. *Kidneys:* Were enlarged, probably one-third. *Brain:* Was not examined.

MICROSCOPIC.—Specimens of the tissue sent us by Dr. Knowlton gave the following findings: Formalin preservation: hematoxylin and eosin.

Heart.—Left ventricle: Cross-section shows much apparent fatty change as seen in the ends of many of the fibers of certain bundles; bundles somewhat widely separated. In longitudinal section striation is everywhere plainly marked and the fibers appear normal. There may be some edema present as the fibers are at times widely apart and the connective-tissue cells stretched from side to side as if by pressure.

Lung.—Many small areas of atelectasis; hyperemia; no general edema; no inflammatory reaction anywhere.

Kidney.—Intense diffuse parenchymatous nephritis and well-marked glomerulitis. Considerable fatty changes in the affected tubules pretty generally. No interestitial nephritis.

Liver.—Organ so fatty as to be barely recognizable; nuclei of cells greatly diminished in number. Blood channels barely discernible.

Spleen.—Hyperemic; on this account some of the Malpighian bodies are much lessened in size and less well defined.

Pancreas.—Apparently normal.

Intestines.—*a*) Small: Solitary follicles are markedly hyperplastic with invasion of small round cells into the neighboring mucosa accompanied by necrosis of epithelium of glandular structure. Much hyperemia.

b) Large: Considerable hyperemia; in two small foci are evidences of a mild degree of round-cell infiltration, with epithelial desquamation, mucoid degeneration of epithelial cells, and edema.

THE CAUSE OF MILKSICKNESS.

a) **Mineral Theory.**—One of the earliest views regarding causation was that some poisonous metallic substance was present in the soil of the affected region and that this was taken up by the vegetation, and caused poisoning in grazing animals. This was the view held by observers in different localities; for example, in Alabama (Shelton, 1836), Indiana (White, 1836), and Kentucky (McAnelly, 1836). One of these writers (McAnelly), who believed that the poison was contained in water as well as soil, would account for the autumnal incidence of the disease by the explanation that the water in wells is usually at its lowest level in the fall and consequently the poison is "more concentrated."

Arsenic and copper were the two substances most commonly accused of being the responsible elements. Seaton (1842) held strongly to the arsenical hypothesis, but his argument was neatly summarized by Drake (1842) in the following words: "Cattle die of trembles—a cow died from taking arsenic, *ergo* the trembles are produced by arsenic," a mode of statement not inapplicable to the conclusion drawn by some other experimenters. Strong ground against the mineral theory is taken by Yandell (1852) who asks: "Who can believe that the flesh of cows may be so saturated with arsenic or copper or the salts of mercury as to kill hogs, dogs, and buzzards?" None of the writers appear to have made systematic tests for the presence of poisonous minerals in soil or in the bodies of dead animals.

The facts of geographical distribution do not favor the hypothesis of a dependence of the disease upon a particular constituent of certain soils. Milksickness occurs both in the glaciated region of Ohio, Indiana, and Illinois, and in the non-glaciated states of Kentucky and Tennessee. We have compared carefully the areas of past and present prevalence of the disease with geological maps of the affected regions and are able to state positively that there is no connection between the geological and chemical character of the underlying rock and the geographical distribution of the disease. In the state of Kentucky, to take only a single instance from the mass of data that we have examined, there are records of the occurrence of milksickness on the Orthovician Formation (Boone and Campbell counties), the Carboniferous (Monroe and Todd counties), the Silurian (Henderson and Davis counties), and the Quaternary (Graves County).

A new turn has been recently given to the theory of mineral poisons by Moseley (1908) who has fed rabbits with aluminum and magnesium nitrate and also with *Eupatorium ageratoides*, the ash of which contains these salts.[1] According to this writer some of the symptoms of trembles were produced in this way.[2] The experiments and their explanation were seemingly suggested by the observations of Crawford (1908) on barium as a cause of loco-weed disease. Full details of clinical symptoms and pathological change have not yet been published. We have not ourselves attempted to repeat these experiments with mineral substances, but we have made thorough search for poisonous ingredients in the organs of one fatal human case of milksickness. No arsenic, copper, mercury, or barium was found in the stomach contents or spleen. A complete mineral analysis of the liver showed only the following metals present: Fe, Ca, Mg, Na, and K. An analysis, including spectroscopic examination, of the incriminated butter (Morris case, p. 417) showed Na as the sole metal present; no trace of Al or Mg was found. Our observations, therefore, so far as they go, lend no support to the theory that trembles and milksickness are due to mineral poisoning.

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[1] Both Mg and Al appear, however, to be not uncommon constituents of plant ash (Czapek, *Biochemie der Pflanzen*, 2, pp. 796–99).

[2] When aluminum and magnesium salts are taken into the human alimentary tract, commonly no symptoms of poisoning are observed (Cushny, *Pharmacology and Therapeutics*, 1903, 3d ed.).

b) Poisonous-Plant Theory.—The connection of the disease with particular areas and seasons, and perhaps also certain other epidemiological features, has caused numerous writers to adopt the theory that some poisonous plant eaten by cattle is the cause of trembles. There has been no universal agreement, however, as to what particular plant should be held responsible. The poison ivy (*Rhus toxicodendron*) and the white snakeroot (*Eupatorium ageratoides*) have been most commonly accused, but numerous other plants have been suspected. In certain localities and at various times the following plants have been held to cause trembles: *Lobelia inflata* (Indian tobacco), *Bignonia capreolata* (cross-vine), *Apocynum cannabinum* (Indian hemp or Indian barley), *Caltha palustris* (marsh-marigold), *Euphorbia esula* (spurge), *Aethusa cynapium* (fool's parsley), "*Vitis hederaceae*," now *Psedera quinquefolia* (Virginia creeper), "*Symphoria glomerata*," now *Symphoricarpos orbiculatus* (Indian currant), *Cicuta* "*virosa*," probably *C. maculata* (cowbane). In the Pecos Valley, N. M., we found that the rayless goldenrod (*Bigelovia rusbyi*) was believed by some to be the cause of the "alkali poisoning" observed in cattle, altho at the same time we were told by many cattle-men that the disease was known among cattle grazing on certain spots where "nothing grew but salt-grass" (*Distichlis spicata*).

The poison-ivy theory at one time obtained wide currency, apparently largely through the publicity given it by Drake (1836 and 1841), and is often referred to as Drake's theory. This author, however, seems himself to have been somewhat lukewarm in his advocacy of it. He says (Drake, 1840), "that this plant (*Rhus toxicodendron*) is the cause of trembles . . . . may be said to be the *popular* opinion of the district." Drake then declares that this opinion is "highly probable" altho he forthwith admits that "there is no conclusive evidence of a single case of trembles having been produced by the Rhus." Among other writers expressing a more or less strong belief in the poison-ivy theory are Travis (1840), Cook (1857), Chase (1861), and Elder (1874). Barbee (1840) states that he had killed dogs with decoctions of *Rhus toxicodendron*, but makes a similar assertion about *Eupatorium ageratoides*.

Numerous writers oppose the theory that trembles is a Rhus intoxication. Some, as Henry (1854) and Beach (1883), point out that horses, cattle, and sheep frequently eat the tender foliage of this plant with relish and evince no signs of injury, while others, as Landrum (1861) and H. M. K. (1862), call attention to the entire absence of milksickness in numerous localities where the poison ivy grows in profusion. The supposed relationship of white snakeroot (*Eupatorium ageratoides*) to milksickness has been recently discussed by Crawford (1908) and need not be fully considered here. Barbee (1840), Dewey (1856),[1] Jerry (1867), Townshend (1883), and Moseley (1906) recount feeding experiments which in their opinions establish etiological relations between Eupatorium and milksickness, but Beach (1883) and many others state that cattle frequently eat this weed without any obvious ill effect. The white snakeroot does not grow in New Mexico where we observed typical trembles in cattle. Crawford's painstaking experiments upon various susceptible animals and upon himself afforded no evidence that the disease is due to any constituent of *Eupatorium ageratoides*. Moseley's recent modification of the Eupatorium theory is referred to above.

Other plants are mentioned as the possible or probable cause of the disease by McCall (1822), Short (1840), Fisher and Kennicott (1861), and Allen (1878), but the evidence adduced is, if anything, more inconclusive than that already cited in the cases of Rhus and Eupatorium. Coleman (1822) experimented in regard to the poisonous qualities of certain plants, but was unable to find any that would produce the peculiar symptoms of the disease. Crookshank (1826) argues strongly against the poisonous-herb theory, but J. N. Smith (1837) and McNutt (1847), on the other hand, agree with the view that the poison is of a vegetable nature. Winans (1840) and Johnson (1866) are of opinion that the poisonous agent is the mushroom. Slack (1854) and Nagle (1859) believe the cause to be a "fungus production" on grass or grass seeds, the first-named author comparing milksickness to ergot poisoning. It is worth noting that in some localities cattle and horses affected with ergot poisoning are said to be "alkalied."[1, 2]

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[1] This writer's observations apparently refer to the white snakeroot, but he did not take the pains to identify the plant upon which his observations were made, altho he adds remorsefully, "I intended to have learned to what class in botany this plant belongs before this meeting, . . . but have been prevented by procrastination."

c) **Microbic Theory.**—Many of the earliest observers felt dissatisfied with the explanations of the causation of milksickness current at the time they wrote. This feeling is manifested by the promulgation of various fantastic hypotheses, some of which have been cited, and especially by the frequent comparison of milksickness to malaria and the ascription of the former to a "miasmatic origin." Wright (1877) after a discussion of the subject concludes "that the cause of the sick stomach is still somewhat doubtful, and will remain so, so long as it is sought for amongst the vegetable or mineral poisons." Reed (1866), after recounting the failure of chemical analyses to show the presence of a mineral poison and of botanical researches to reveal the existence of a specific poisonous plant, remarks, "What success may be had in searching for a cryptogamic or animalcular cause remains to be shown." De Bruler (1858) is forced to believe

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[1] *Breeders' Gazette*, September 25, 1907, p. 572.

[2] *Miscellaneous theories.*—Hardly any remotely plausible hypothesis of the cause of milksickness is without advocates. Many writers claim that a strong resemblance exists between this disease and malaria, (Lescher, 1850; Thompson, 1853; Sale, 1878; Rawlings, 1874; Dorsey, 1876). Lea (1821) exprest his belief that the disease was due to a "miasmatic exhalation." Horne (1846) believed that the "exciting cause" of milksickness and yellow fever is the same and that "the agent is miasmata." Wozencraft (1873) maintained that the disease was due to "an exhalation from the soil." Jones (1862) states his somewhat inclusive opinion as follows: "I conceive the cause of this disease to be a peculiar miasma, generated under peculiar circumstances. It may be an animal sporule; a vegetable atmospheric fungus; or a gas formed by a particular combination of the elements." The same writer adds: "We generally, I may say invariably, find milksickness in or near a notoriously miasmatic district."

Kennedy (1878) thinks that he detects a similarity between the disease and the tsetse-fly disease in Africa described by Livingstone, and accordingly attributes milksickness to the bite of a "certain fly." Achelor (1884) likewise ascribes the disease to the bite of "the milk sick fly," an insect he does not further differentiate. Carpender (1884) and Murfin (1884) vigorously attack Achelor's fly theory.

An anonymous writer (S., 1829) in the *Transylv. Jour. Med.* refers to experiments made about 1800 which gave rise to the conviction that the disease was occasioned by cattle eating "the mass of vegetable matter growing in the bottom of stagnant pools of water." Jackson (1881) attributes the disease to the "seeds of a vegetable." Thompson advances the view that milksickness may be due to an "excess of carbonic acid floating in the atmosphere," and so would account for the greater prevalence of the disease in dry seasons by the premature falling of the leaves (which remove CO_2 from the atmosphere). Another writer (S. M. B., 1892) has no hesitation in asserting that the disease is caused by swallowing the web of the spider. "It is an admitted fact that a spider web when fresh is poison, but a little sunlight and heat rob it of its virulence, and it becomes an inert absorbent." There seems no need to push historical inquiries any farther.

that the poison is not vegetable or mineral, and continues: "But there is a large class of animal poisons commonly called infections which do possess the power of self-propagation, whenever they are placed in a proper condition for such development." He cites hydrophobia as an illustration and adds: "Infectious diseases are sometimes the results of animalcules. May they not always be produced in the same way?" Woodfin (1878) is also inclined to believe that the disease has an animalcular origin. Philips (1877) who was evidently strongly under the influence of the germ theory of disease points out that milksickness is a specific infection, that it has an incubative period, is transmissible, and reproduces its kind. He reports observing in freshly drawn blood and in urine "a great number of living, moving, spiral bacteria." Logan (1881) exprest his belief that the disease is due to a "*contagium vivum*," without, however, giving any specific observations in support of his opinion. About the same time Gardner (1880) reports seeing "countless multitudes of actively moving, writhing, twisting bacteria" in the blood of a sick heifer and also in the blood of two human patients. A fungus (*Sterigmatocystis*) has been obtained by Hessler (1905) from the blood of a sick horse.

EVIDENCE IN FAVOR OF THE MICROBIC THEORY.

Epidemiological Resemblance of Milksickness to Anthrax.—There is a close correspondence between the epidemiological features of milksickness and those of anthrax in cattle. As shown by Friedrich (1885) anthrax is primarily associated with infected pasture land and occurs most commonly in certain well-known localities. Its prevalence in particular regions (e. g., the Bavarian Alps) is dependent in the first instance on variations in soil moisture and is hence affected by seasonal differences in temperature and rainfall. Friedrich emphasizes the influence of drainage in diminishing the amount of anthrax. "Wenn es gelang, den Milzbrand aus einer Gegend zu vertreiben, oder doch zu reduciren, so ist dies nur der Trockenlegung der versumpften Milzbrandlocalitäten zu verdanken. So verschwand der Milzbrand nach Flussregulirung, oder er nahm ab, als man die gefährlichen Weiden in Ackerboden umwandelte." According to Bollinger (1885) in the Bavarian Alps anthrax is "eine exquisite Bodenkrankheit," and is most likely to occur when a wet year is followed by a less wet or a dry year accompanied by high temperature. These statements, as shown in the foregoing sections of this paper, apply equally well to milksickness. The persistence of both milksickness and anthrax in given localities is dependent in some way upon the content of soil moisture. Bürger (1825) long ago drew attention to another analogy between milksickness and anthrax, both diseases, as he expresses it, being communicated through milk and meat. Recent writers and bibliographers generally accept the theory of a parasitic origin (Maurel, 1889; Boggs, 1907); Crawford, 1908; McCoy, 1907. Certain facts already set forth respecting the nature of the virus strongly support the microbic theory. Such are the destruction or weakening of the virus by heat, the apparent connection of the virus with particular tracts of soil while adjoining areas that are chemically and botanically similar are entirely free of it, and especially the self-propagating power of the virus which has been long recognized as one of its most characteristic properties.

Our own observations bear upon the microbic theory and may now be described in detail. The first cases of the disease coming under our notice were in New Mexico. Blood films, which were made from a human case (above, p. 456) and stained by the Romanowsky and other methods, did not show the presence of any microorganisms. Agar tubes inoculated with the blood from the elbow vein gave no growth. The case was quite far advanced in convalescence. A young bull apparently in the early stages of trembles was shot and an autopsy made while the body was still warm (rectal temperature 103.2°). Agar tubes inoculated with bile and with heart blood gave no growth. Rabbits inoculated with serum (intraperitoneally, 1.5 c.c.) and with bile (subcutaneously, 2 c.c.) remained well.

Following these preliminary experiments we had the opportunity of making a more thorough examination of the body of a young pregnant heifer five hours after death. Coverslip films were made from spleen, liver, kidney, heart blood, lung, and gall-bladder, and from the liver of the fetus (four months ?). In the films from all the organs a long slender bacillus, staining uniformly with methylene blue, was found in very small numbers (1 to 8 per film). No bacteria were found in the films made from the heart blood. Plate cultures were made on agar with heart blood, liver, spleen, kidney, and fetal liver; two tubes of slant agar were inoculated with two or three loopfuls of bile removed from the gall-bladder after careful searing. After 12 hours' incubation at 32° C. the agar tubes showed profuse growth. Films stained with methylene blue showed apparently pure culture of a bacillus with deeply stained metachromatic granules and round terminal spores.

On the agar plates, after 36 hours' incubation at 32°–36° C. a few small irregular, transparent colonies appeared. There was an average of about six colonies to a plate; the plate from the spleen showed a mixture of colonies; the others were apparently a pure culture. Bacilli from several colonies were stained and examined microscopically and were morphologically identical with those found in the bile cultures. Pure cultures were eventually obtained from the plates made from the liver and fetal liver and they were in every respect identical with the microorganism found in the bile. A young rabbit (about 400 gm.) was inoculated intraperitoneally with 2 c.c. of heart blood from this heifer; the rabbit died in four days and the same bacillus discovered in the bile and in the fetal liver of the heifer was found in pure culture and in large quantities in the peritoneal exudate. Two rabbits inoculated, respectively, with the peritoneal exudate (0.75 c.c.) and heart blood (1.5 c.c.) of this rabbit also died. The bacillus thus discovered in the organ of a fatal case of "alkali poisoning" or trembles has since been found by us in every case of the disease that has come under our observation. The preceeding list gives our findings in detail. In several instances the bacillus was

PRESENCE OF B. LACTIMORBI.

Animal	Organ or secretion
Heifer P_1	liver
"	bile
"	spleen
Fetus	liver
Heifer P_2	bile
Steer P_1	intestinal contents (mucus)
Heifer P_4	intestinal contents (mucus)
Horse$_1$	gut nodule
"	pericardial fluid
Lamb$_1$	brain
Lamb$_2$	heart blood, liver, and peritoneal fluid
Child H. J.	spleen
"	duodenal contents
"	pericardial fluid
Man M.	feces
Man H.	"
Man A.	"
Cow R.	milk
Cow P.	"

present in pure culture, namely Heifer P_1, bile, and fetal liver, Heifer P_1, bile, Horse$_1$ gut nodule, intestinal wall and pericardial fluid. In other cases it was accompanied by *B. coli* or rarely by staphylococci. We have designated this bacillus as *B. lactimorbi.* As we have elsewhere (Jordan and Harris, 1908) described the character of the bacillus with some fulness we will simply quote the essential points of that description here.

DESCRIPTION OF BACILLUS.

The morphologic and tinctorial features of this specific organism may be briefly given as follows: In coverslip smears from the organs the bacilli are longer and more slender than the colon bacilli, and stain occasionally unevenly with methylene blue. (Fig. 5.)[1] In preparations made from cultures grown on agar at 37° C. the organism is found to be a rod a little smaller than the anthrax bacillus, occurring singly and in pairs and in occasional filaments. As a rule the rods at the end of 24 hours' incubation do not stain deeply with methylene blue, even if heated for a moment or two over the flame, but at one or both poles or at the center of each rod are found metachromatic granules which take on a reddish or purple tint, standing out sharply from the rest of the stained rod. In young culture the bacilli are gram-positive but the granules are not differentiated by the gram stain. Spore-formation was observed in our first culture, the spore being perfectly round and situated at one pole of the rod in the mature forms; in the less mature rods, 24 hours old, the spore may be slightly oval and lie not quite at the end of the rod; the general effect produced by the shape and location of the spore reminds one strongly of the tetanus bacillus (Fig. 6). Rarely one rod may show bipolar spores.

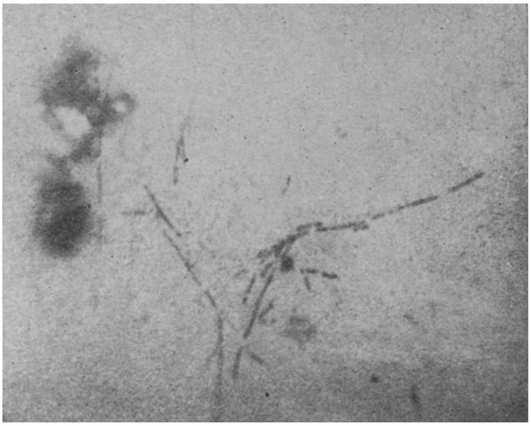

FIG. 5.—*B. lactimorbi.* Smear, peritoneal cavity, Rabbit 5. Methylene blue. ×1100.

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[1] For the preparation of the photomicrographs we are under obligation to Mr. A. C. Hicks, Assistant in Bacteriology.

The spores stain readily by any of the ordinary methods. The organism is motile and it is found on staining by van Ermengem's method to be possessed of 10 or 15 flagella disposed peritrichally, the flagella measuring in length about five times the length of the bacillus itself.

This bacillus grew on our plates as small streptococcus-like colonies. It was soon found that some of the bacilli isolated and possessed of similar cultural characteristics did not answer in all respects to the description just given. Some differed markedly in morphology, forming more filaments than rods, both being almost devoid of metachromatic granules and in some cases even of spores, although corresponding culturally. This morphologic deviation occasioned some perplexity until it was found that if grown on gelatin at 25° or 30° C. the refractory bacilli would become metachromatic and sporogenous. We were able at the outset to establish the presence of *B. lactimorbi* in the cultures from four animals from the following sources: In the intestinal contents of two cows, in the bile, spleen, and liver, and in the liver of a four months' fetus of another (intestinal contents not examined), and in the pericardial fluid and intestinal nodule of a horse.

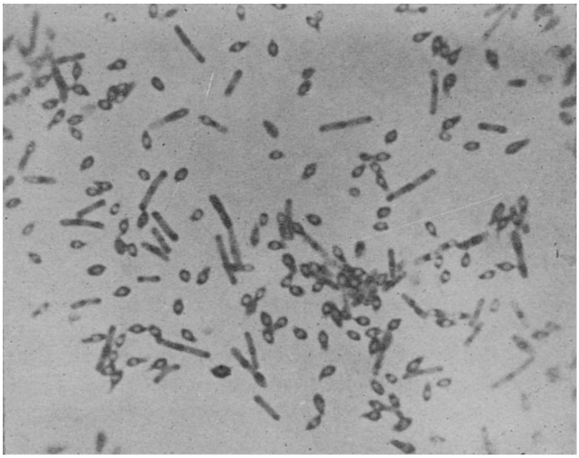

FIG. 6.—*B. lactimorbi*. Pure culture from P. H. 1, bile. Six-day growth in Jordan's asparagin solution. Methylene blue. ×1100.

Studied in greater detail after we had become assured from the results of animal inoculation that we were in possession of a pathogenic microorganism, the following appearances and cultural reactions were observed:

Agar slant.—At 37° C. at the end of 24 hours, the surface is more or less irregularly covered with a delicate veil-like growth, which is more profuse at the end of from 48 to 72 hours and eventually may take on a semiviscid character in some cultures; color, grayish, moist, smooth, and glossy; no pigmentation of the growth itself or of the medium; no gas; condensation-water growth heavy, gray-white in color. No odor.

Dextrose-agar stab.—Surface growth occurs around the puncture and extends irregularly around from it in a delicate manner. At first the bacterium grew sparingly down the middle track for about 1.5 cm. but now it grows down 3 or 4 cm. or even farther; the needle growth is smooth and delicate, whitish in color and smooth; no pigmentation of the medium; no gas; no odor. The growth is more luxuriant after a few days.

Broth.—At the end of 24 hours there may be not any growth noticeable except sometimes a slight clouding of the broth at the surface. At the end of 48 hours there is seen on the surface, a well-formed pellicle, which will sink if the tube is agitated; the rest of the medium is feebly clouded and there may be a fine semiflocculent sedimented growth at the bottom of the tube or along the dependent side, if the tube has been inclined.

Litmus milk.—If not heavily seeded there may be no visible signs of growth. As a rule there is no change at the end of 48 hours; by 72 hours the cream ring will show a delicate green-blue color in the drier parts, and even in some instances the upper portion of the milk will show a slight alkaline reaction; this reaction daily increases until at the end of ten days the whole tube takes on an alkaline reaction which becomes more and more marked until as in cultures of the hog-cholera bacillus the medium may lose a part of its color, turning a dirty white, and even begin to turn opalescent, indicating a solution of the casein due to the great increase in free alkali. Coagulation has not been observed.

Potato.—No growth was observed; no multiplication was apparent on examining the surface by scraping and staining the scrapings and examining them under the microscope.

Heinemann's synthetic potato medium.—No visible growth could be made out even at the end of two weeks; microscopic examination of the scrapings of the medium at the end of two or three days shows evidence of abundant multiplication.

Blood serum (Löffler's).—At the end of 48 hours there occurs along the needle track and confined to it an elevated, fairly vigorous, smooth, moist, yellowish, glossy growth, which later tends to spread but little. There is no discoloration of the medium, nor any liquefaction, nor odor.

Gelatin stab.—Grown at 20° C. growth begins to appear at the end of 48 hours, but is not sufficiently advanced for description until 72 hours old; then there is seen little or no surface growth around the puncture; down the stab to the extent of about 2 cm. a delicate gray, smooth growth appears. At the end of a week the surface growth has become extended on all sides from the puncture as a fairly well developed film of a whitish color, smooth, moist, and glossy; at times the first evidences of liquefaction may now be detected, but this is not well established until the tenth day, when the medium just beneath the surface growth is slightly fluid. As time passes the liquefaction slowly progresses, extending down the stab to a slight degree, the gelatin at the end of 18 days or three weeks being liquefied completely across the tube and slightly downward. If kept at 23° or 24° C. the appearance and progress of the liquefaction makes more rapid headway, and at the end of a month at this temperature the whole of the gelatin may be reduced to a fluid state. There is always noticeable a more or less well defined putrescent odor.

Gelatin.—If the organism is grown in a petri dish of gelatin at 30° C., it is found at the end of 24 hours that the whole of the medium is quite cloudy, with not infrequently several small islets of pellicular material scattered over the surface. The surface-growth increases during the next four days but never forms a complete film over the surface. The putrescent odor is more manifest in cultures grown at this temperature (30° C.).

In all cases in which a surface film forms at room temperatures on any of the media, fluid or solid, and particularly in gelatin left at 30° C. spore-formation is abundant.

When grown at 37° C., particularly at the first isolation, the organism presents certain noteworthy differences both in growth appearance and in morphology. On slant agar the growth may continue thin and veil-like or may be as vigorous as the growth of the typhoid bacillus on the same medium. In broth there may or may not be a pellicle; as a rule at the end of 48 hours, there is a slight cloudiness only and a tolerable amount of sediment in the tube, which increases only slightly thereafter. The alkalinization of the milk cultures is not hastened by growing at this temperature. The morphologic alterations are striking; the size of the bacillus is less, approaching that of the typhoid bacillus, and there are irregularities in staining both in the individual cells and in different cells in the field; filament-formation is more pronounced, and there may even be swollen, twisted forms of a shape entitling them to be classed as involution forms; metachromatic granules may be entirely absent or a few cells containing them may be found after prolonged search; spores are sometimes formed but as a rule not so abundantly as at 30° C. and by some races not at all. If a culture with these characteristics is grown on gelatin at 20° C. or at 30° C. and allowed to pass to the stage of liquefaction and again grown on the same medium and at the same temperature the type with metachromatic granules and abundant spore-formation is produced. Our recognition of the true nature of certain cultures was considerably retarded by the uncertainty introduced through this polymorphic tendency.

Agar-plate colonies of *B. lactimorbi* at the end of 24 hours at 30°, or 37° C., resemble those of *Strept. pyogenes*, but with this difference that they show a tendency to spread out in a film, particularly if the agar is freshly made, when the whole surface of the plate may be covered; film formation is also to be noted on the lower surface of the medium against the glass bottom. One of the strains at the end of three days on agar at room temperature developed a very distinct yellow color both in the depths of the agar and on the surface. In gelatin plates grown at 20° C. at the end of from 43 to 72 hours the colonies make their appearance and resemble at first those of streptococci but at the end of the fourth day they appear more vigorous, the surface colonies partaking more of the characteristics of *Staph. albus*, altho the color is of a yellowish-white and they are not so elevated nor large, measuring about 2 mm. in diameter. Liquefaction becomes apparent at the end of ten days or two weeks, the colonies settling down in the medium which after five or six weeks becomes almost wholly liquefied.

The thermal death-point of the bacillus as determined by the use of Sternberg's bulbs varies according to the type of culture employed, as shown thus:

48-hour agar culture grown at 30° C., fully sporing......	15′ at 100° C.
48-hour agar culture grown at 37° C., non-sporing.......	5′ at 55° C.

All tests were made with a time limit of 90 hours' incubation in the thermostat at 37° C., using agar as the medium for growth.

Agglutination.—Our first experiments upon agglutination gave negative results (Jordan and Harris, 1908), but later observations have shown that under some conditions agglutination occurs. Human serum from two of the Altamonte cases ("A" and "M") agglutinated the bacilli from one of the other cases ("H") in 1:50 dilution (microscopic method) and also strains from the organs of a lamb (Morrow) and from Altamonte soil. One of the sera ("M") agglutinated *B. lactimorbi* obtained from the milk of one of the cows presumably concerned in the production of the Altamonte outbreak; the other serum ("A") had no effect upon it. Cultures from one of the New Mexico cattle, and from soil in Ohio were unaffected by either serum.

Another test with human serum ("H. J., Morris") gave a distinct agglutinative reaction upon two strains of *B. lactimorbi* (macroscopic method, 30 min. at 37.5°) in dilutions of 1:50 and 1:200, while the 1:500 dilution showed only a slight agglutination, hardly more than the trace of spontaneous flaking observed in one of the controls. This serum did not agglutinate *Bacilli typhosus*, *paratyphosus* **A,** and *enteritidis* Gärtner in dilution of 1 in 50.

Distribution of *B. lactimorbi.*—The striking and somewhat peculiar character of the microorganism we have isolated enables its presence to be rather easily detected and its identity quickly determined. Since we were not able to find in the literature any description of a bacillus possessed of the characters of *B. lactimorbi*, even in special studies of aerobic spore-bearing bacilli (Ford, 1901), we were at first led to believe that a peculiar and highly localized distribution of *B. lactimorbi* in the soil of certain districts might explain the singular geographical incidence of milksickness. This has not proved to be the case: we have found *B. lactimorbi*, or a bacillus not distinguishable from it by any of the tests we have applied, in the soil of regions where milksickness has never been known; we have found it in normal cow dung, on various grain and forage plants, and in some other locations. We have not been able to demonstrate that the bacillus is present in any greater abundance in the soil of milksick localities than elsewhere and altho it may appear remarkable to others as it does to us that a bacillus so widely distributed and with such highly distinctive characters as *B. lactimorbi* should have so long remained undescribed; nevertheless such seems to be the case.

If infection of grazing cattle with *B. lactimorbi* occurs, it therefore must depend more upon the occurrence of pathogenic races or varieties than upon the presence of the widespread non-pathogenic or slightly pathogenic stock.

Animal Experiments.—Rabbits, guinea-pigs, dogs, cats, lambs, and calves have been used by us in experimental work.

Rabbits.—A young rabbit (R. 1), weighing about 400 gm., was inoculated intraperitoneally with 2 c.c. of heart blood from a heifer that had died of "alkali poisoning" five hours previously. The rabbit to all appearances remained entirely well for four days, at which time a certain listlessness was noted. On exercising the animal it quickly became exhausted and after running a short distance would fall over and then slowly struggle to its feet, panting vigorously. The muscular weakness increased during a period of about five hours after this condition was noticed, and the animal then died quietly. The autopsy disclosed a general exudative peritonitis, the exudation being whitish-yellow and fibrinous everywhere, all organs being more or less covered by it. The liver was very much enlarged, dark red, soft, and friable. On section the lobules could not be readily distinguished (cloudy swelling). The spleen was enlarged, deep red, and soft, the Malpighian bodies being barely discernible. The kidneys were enlarged, moderately red, and showed cloudy swelling. In portions of the small intestine the vessels were prominently injected, but there were no ecchymoses. The heart was apparently normal.

Bacteria found: Coverslip films made from the peritoneal exudate, heart blood, liver, and intestinal mucus showed in all cases long slender bacilli with the morphologic character of *B. lactimorbi;* in the intestinal mucus other forms were also present. Plates made from peritoneal exudate and heart blood gave pure cultures of *B. lactimorbi.*

A second rabbit (R. 2) was inoculated intraperitoneally with about 1.5 c.c. of the clot in the heart of R. 1 rubbed up in sterile water. Unfortunately this rabbit died during our return journey to Chicago (about 3 days after inoculation), and before we were able to make an autopsy decomposition changes had gone so far that the material was virtually worthless. Other rabbits (adults) have been fed with pure culture of *B. lactimorbi* and also inoculated subcutaneously and intraperitoneally, but up to the present with negative results.

Guinea-pigs.—A number of guinea-pigs have been fed and injected with pure cultures of *B. lactimorbi,* for the most part with negative results. In a few instances, however when animals were used that had previously been weakened by other treatment, for example, by injection with diphtheria toxin-antitoxin mixtures, death occurred. No characteristic changes could be certainly observed in the organs, but in one case (G.-P. 8.) *B. lactimorbi* was isolated in pure culture from the liver, plates made from the heart-blood and bile of the same animal showing no growth.

Dog 1.—From January 28 to March 5 this animal received agar and gelatin-plate cultures of *B. lactimorbi* from steer P. in nine doses. On March 8 it received three gelatin-plate cultures. This animal was a rather old dog, fat, lazy, and docile. Ten days after the first feeding it was noticed that its appetite was not so good as usual. Two days later it passed some masses of hard feces with a small quantity of bloody mucus. On examining this mucus bacilli were found in good numbers along with cellular débris. When the bacilli were stained with methylene blue they showed metachromatic granules, but there were no spores present. Plated in agar the material yielded the typical *B. lactimorbi,* and abundant spore-formation was observed. Eight days later the animal again passed a considerable quantity of bloody mucus when out for exercise on the street in care of an attendant; no cultures were obtained, and it was not observed to pass any further mucus. Four days after the mucus was first observed the animal was noticeably thinner and showed well-marked irritability which as time passed developed into an almost maniacal raging when the cage was approached, altho when out for exercise it was quiet enough, except to actual strangers at whom it snapped when they attempted to pet it. February 27 it was in a decidedly weak and emaciated state. It also had a marked limp in the left forefoot, but on examination of the paw no foreign body could be found. On extending the leg evidence of pain at the shoulder joint was given, altho there were no external manifestations at that point. By February 29 the dog for the first time failed to leave its box voluntarily. On March 1 there was very definite weakness and stiffness in the hind legs. Its bark became harsh and husky and the conjunctivae were quite deeply injected. This condition marked the height of the clinical manifestations, and since the animal became no worse it was killed by chloroform on March 10 and an autopsy made immediately.

Abdominal cavity.—On opening the peritoneal cavity there are no signs of inflammation anywhere. The liver is definitely enlarged; general color a deep chocolate, in places somewhat mottled by lighter-colored areas; there is much blood in the organ, but on pressing this out the liver takes on a yellowish cast due to a moderate grade of probable fatty change in the parenchyma; consistency soft, capsule and liver substance rupturing easily on handling. On section the liver lobules are not clearly marked out and there is some cloudy swelling present as well as some fatty change; no focal necroses are seen; the tissue contains much blood; color red brown. The gall-bladder and bile seem to be normal. Spleen is probably normal in size; color dark red. Malpighian bodies near surface are readily seen; consistency is about normal. On section, it contains considerable blood, but one can detect the Malpighian bodies without difficulty. Kidneys appear to be normal, both outwardly and in section. Adrenal glands look normal and on section are pale. Small intestine is injected in some places, but not markedly so; Peyer's follicles look prominent as seen from the outside; the mesenteric glands are not enlarged or altered; large intestine is apparently normal and in places contains fecal matter. On opening the whole gut there is some injection of the mucosa of the small intestine, but in only a slight degree; no ulceration and altho Peyer's patches appear a trifle prominent there is no sign of inflammation in them. There is present a large number of a species of tapeworm. The large intestine shows no demonstrable lesions. No ecchymoses can be found in the serous membrane of the cavity. Bladder is not injected and is apparently normal.

Thoracic cavity.—No fluid or ecchymoses are present in the pleural cavities, and no signs of inflammation. Lungs are light in color and apparently normal. Heart is a trifle large for a dog of its size (20-lb. dog), walls of both ventricles are pale and soft; valves are free of inflammatory changes; endocardium is clear; pericardium is clear and shows no ecchymoses.

Brain.—Cortical vessels are somewhat injected and full; no signs of meningitis. On section, no injection of the vessels was found, ventricles appear normal, with a slight trace of clear fluid in them. Cerebellum and pons and medulla are seemingly in a normal state.

BACTERIOLOGY.—Coverslips and cultures in agar were made from the liver and kidney. The coverslips showed nothing characteristic; from the agar plates, from both liver and kidney, *B. lactimorbi* was isolated in pure culture after 48 hours' growth.

MICROSCOPIC. *Liver.*—The whole section shows evidence of cloudy swelling, but more particularly are the cells of the middle and central zones of the liver lobules severely affected; the cells are greatly increased in size, take eosin strongly, and their protoplasm appears in minute round granules of colloid-like material and occasionally contains fat globules. Despite the protoplasmic changes the nuclei in general take the hematoxylin well; only occasionally do they appear vesicular and staining poorly, or are absent. Capillary vessels and central veins are full of blood and distended.

Spleen.—Slightly hyperemic; otherwise normal.

Colon.—Appears normal.

Kidney.—Very hyperemic; otherwise normal.

Heart.—Normal.

Cerebrum.—Normal.

Small intestine.—Hyperemic; otherwise normal.

Dog. 2.—A young dog of some fifteen pounds' weight, in good condition was received on February 16, and during the interval between this date and March 19 it received four doses of gelatin-plate cultures of several different strains of *B. lactimorbi.* On February 29 it was noticed that the animal had become noticeably thin, altho lively and active. On March 10 it was much thinner and perceptibly weak, remaining contrary to habit in its box, after entrance of anyone into room. Next day it had developed a bronchitis, causing it to cough and interfering with its barking. On March 12 it was evidently very ill, lying in its box and showing great disinclination to rise; March 17 found it still in an enfeebled state, unable to bark, and the cough still continuing. On March 19, however, it appeared much better and was out of its box; the cough was less severe. On March 20, it barked vigorously; the cough had almost disappeared, and the animal was lively. It was killed by chloroform and an autopsy was performed at once.

Nothing of note is revealed by inspection. Reflection of the skin shows that the dog is exceedingly emaciated, there being no subcutaneous fat present. The muscles everywhere are very pale red. The inguinal and axillary glands are of normal appearance.

Abdominal cavity.—On opening the abdominal cavity the peritoneum shows no signs of inflammation nor ecchymoses. The liver does not appear to be enlarged; color light chocolate-brown; firm to the feel of the hand; it does not appear to show cloudy swelling or fatty change, and does not contain any excess of blood. No focal necroses are seen through the capsule. The gall-bladder is empty. On section the liver looks in a tolerably healthy state, as does the gall-bladder. The spleen is normal in appearance, both in the cut and uncut condition. In similar way the kidneys are likewise in an apparently good state. Adrenals are normal. The small intestines are found to be empty, and in places a bare trace of injection of the outer coats can be found. The large gut is seemingly in a healthy state and contains some fecal material. On opening up the intestinal tract, it is found that the small gut contains a fair amount of bile-stained mucus, and there is seen an occasional slight swelling of a Peyer's patch, but no sign of inflammation; there is an entire absence of any past or present sign of necrosis anywhere in the gut. The large gut contains soft feces and is in a normal state. Stomach apparently normal.

Thoracic cavity.—The heart looks of proper size and is not soft to the touch, but the muscle of the ventricles is somewhat pale. Valves and endocardium are normal. The lungs show a few small points of atelectasis in the dorsal portions of the lobes of each; no trace of any bronchopneumonia. Trachea shows in its walls and in the wall of some of the larger bronchi some few flakes of muco-pus, altho there is lacking any of the signs of active inflammation. Brain and spinal cord are in a normal condition.

BACTERIOLOGY.—Coverslip preparations were made from the liver, intestinal mucus, and muco-pus of the trachea. That from the liver showed no bacteria; that from the intestine a number of colon-like bacilli and a few cocci; in the tracheal pus there were quite a number of lanceolate diplococci and a very few bacilli. Cultures in agar were made from the liver, intestinal mucus, kidney, and heart blood. Liver and heart blood sterile, the intestinal mucus gave *B. coli* and streptococci; *B. lactimorbi* was not obtained.

MICROSCOPIC. *Cerebrum.*—Appears normal.

Cerebellum.—Appears normal.

Small intestine.—Normal.

Kidney.—Normal.

Heart (cross-section).—Normal.

Liver.—Presents diffuse parenchymatous hepatitis of a moderately severe degree with considerable accompanying fat metamorphosis; the nuclear changes are not very great.

Dog 3.—This animal proved unsuitable for experimentation.

Dog 4.—This animal received gelatin-plate cultures of one strain of *B. lactimorbi* on March 19, 23, 29, and April 8. On April 7 it appeared to be less active in its movements, a trifle thinner, and showed no disposition to bark or whine. Next day, altho it barked a little, observers received the impression that it was somewhat enfeebled. On April 9 it was weak and refused to leave its box, and when persuaded to rise up in the box it trembled perceptibly in the forequarters and neck muscles. On April 11, it was lively and again got out of the box and danced about in its cage and wanted to be petted. On April 14 no signs of illness could be further detected. Chloroformed. Condition found on autopsy similar to that observed in Dog 2.

MICROSCOPIC. *Kidney.*—Glomerulitis; exfoliated cells, etc.; parenchymatous nephritis of a mild grade affecting the convoluted tubules and descending loop of Henle. Some of the descending tubules of Henle's loops contain considerable fat.

Liver.—The cells of the whole section are in a state of cloudy swelling particularly so in the middle and central zones of the lobules. The swelling of the cells renders the capillaries less conspicuous than normal. In two localities are seen foci of chiefly polynuclear leukocyte invasion, one much greater than the other, arising from the portal canals; where the leukocytes invade the lobules the liver cells have vanished.

Dogs 5-8.—(See article by A. B. Luckhardt, this *Journal*, p. 497.)

Cats 1, 2, and 3.—These kittens were fed, respectively, with milk from three cows that were on the Altamonte farm at the time of the outbreak (p. 430). The kittens were all puny and in poor condition. Nos. 1 and 3 received about 30 c.c. each, No. 2 about 20 c.c. No. 2 died about three days after the feeding began; the autopsy showed no pathological changes other than those consequent on inanition and anemia. *B. lactimorbi* was not found in the organs or intestinal contents. No. 1 died two days later and manifested a similar pathological condition. The bacteriological examination showed the heart, liver, and kidney to be sterile; the intestinal contents gave

B. lactimorbi together with common intestinal forms of microorganisms. No 3. died twelve days after beginning the feeding. The autopsy notes are as follows: "The only pathological condition (other than great emaciation and anemia) was in the large intestine. The whole intestinal tract was empty; the small gut contained a few round worms and much sticky mucus; there were no signs of inflammation; *the large gut from its beginning to within* 3 *cm. of the anus showed a patchy injection of the mucous coat which was somewhat edematous as well.* The liver was paler than normal, but was of normal consistency and showed no lesions of a macroscopic nature. The spleen seemed a trifle larger than normal and it was difficult to determine whether parenchymatous lesions were present. The heart showed no ecchymoses, but was paler than normal tho not of softer consistency. The lungs appeared normal."

MICROSCOPIC. *Liver.*—Throughout the whole section there are evidences of an existing mild degree of parenchymatous degeneration, the cells having contents of round granular bodies which give a general stain less pronounced than do normal cells; here and there are cells without nuclei, some poorly staining, whilst the majority stain well. In several parts of the section necrotic areas exist into and around which connective-tissue proliferation has taken place and round-celled infiltration; in one or two of these areas some necrotic liver cells can yet be seen. There is no hyperemia present and no cholangitis.

Spleen.—Apart from the presence of blood capillaries lessening the distinctive appearance of the Malpighian bodies the organ seems to be quite normal.

Kidney.—Practically normal; only occasionally is the evidence of a tubule or two showing evidences of parenchymatous degeneration.

Heart (cross and longt.).—In a few places in the specimen do the fibers retain cross striation; most of the fibers in certain bundles are shrunken and contain little stainable substance while their nuclei are swollen, distorted, and stain very poorly. In a number fat droplets can be discerned. In two places there are evidences of interstitial myocarditis with destruction of muscle elements in their locality.

Colon.—Much mucoid change and atrophy of cells of the tubules, with some round cell infiltration and superficial necrosis.

BACTERIOLOGY.—Three days after the milk diet had ceased and seven days before death, a swab culture was made from the rectum and resulted in the isolation of *B. lactimorbi.* At autopsy cultures were made from the small and large intestines, the liver, kidney, and heart blood, but the bacillus was not found.

Cat 4.—A young, active, perfectly healthy animal about 6 months old. Rectal temperature 99.6° F. August 12, fed two slant-agar cultures of *B. lactimorbi* in milk. August 13, apparently quite well. Rectal temperature 102.4. Feeding of August 12 repeated. August 14, appears lively and well. Temperature 101.3. Dosed as before. August 15, very lively but thinner. Temperature 103.4, received same dose as before. August 16, temperature 103.0, mucus noticed on thermometer after withdrawal from rectum, anus reddened. From this date to August 30 (animal killed) daily doses of the same culture were given except on these dates, viz.: August 24, 27, and 28. August 17, temperature 102.6. August 18, slight redness of rectum, no mucus; swab cultures made from rectum evidently caused pain. August 19, lively and active; temperature 102.2; anus considerably reddened; signs of pain when thermometer inserted. August 20, animal shows sign of irritability, is not so active, shows notable weakness of hind legs; temperature 102.4. August 21, temperature 102.6.

August 22, kitten lively and able to run about altho experiences marked difficulty in springing up due to weakness in hind legs; temperature 101.6. August 23, kitten very lively, redness about anus gone, muscular weakness barely perceptible; temperature 101. August 29, temperature 102. August 25, kitten appeared normal, temperature 99. August 26, kitten thin but frolicsome; from the anus there exuded for the first time bloody mucus. Coverslip preparations showed multitudes of morphologically typical polar-staining bacilli thought to be *B. lactimorbi.* Culture showed definitely the presence of this organism. August 27, temperature 98.4. August 28, temperature 99.6. August 29, temperature 99.6. August 30, since August 26, the kitten has been well and lively. Chloroformed and autopsy made; the body seems perfectly normal. Cultures from heart blood and liver were negative (sterile). Kidney and liver preserved in 10 per cent formaldehyde.

MICROSCOPIC. *Kidney.*—Occasionally are found convoluted tubules that show parenchymatous degeneration accompanied by fatty accumulation in the shape of small droplets. In the descending limbs of Henle's loops much the same picture is seen only that the fat drops are relatively large, and at times are often present where no parenchymatous degeneration exists. Glomeruli normal.

Liver.—Generalized parenchymatous hepatitis, in places within the mid or central zones taking on an intenser focal reaction. Accompanying this condition is marked fatty metamorphosis, the fat being usually distributed in the cells as small droplets; in one locality some of the lobules looked like adipose tissue, so much fat did the cells contain. No necrosis found, only a couple of points of round and polynuclear leukocytic infiltration. No cholangitis. No hyperemia.

Cat 5.—Owing to condition of this animal feeding experiments were not undertaken.

Cat 6.—January 16, weight 990 gm. Fed 10 gm. suspected butter (from Carlsbad, N. M.) in warm milk. *B. lactimorbi* was isolated from this sample. No change noted, dose repeated. January 18, dose repeated. No signs of illness. January 19, looks thin and out of condition; weight 990 gm. January 20, has bronchitis; playful, but weak and emaciated; weight 930 gm. January 21, animal found dead in morning, body placed on ice by janitor, but notification delayed. Autopsy at 10:30 A. M., January 23. Body in an excellent state of preservation. The animal showed great emaciation, there being no subcutaneous fat. On opening the abdomen no signs of peritonitis. Liver appeared somewhat enlarged, was not as dark colored as usual, and in many places the lobules were not discernible. It was not particularly friable. On section, the organ did not contain much blood, the lobules were indistinct or not discernible, there being apparently some moderate degree of cloudy swelling. The spleen was dark colored, a trifle soft, and enlarged; on section contained blood; Malpighian bodies not seen. The kidneys seemed somewhat enlarged and waxy looking. On section, the cortex of each was yellowish-white in color, apparently fatty, blood vessels between the bundles plainly seen; the Malpighian tufts not seen. The small intestines, beyond containing much mucus, appeared normal. Large intestine normal. Mesenteric gland at ileocecal-colic region enlarged and pale. Adrenals seemed normal.

Thorax.—Heart: Right side contained much blood; left empty. Muscle looked pale and was soft. Valves normal. No ecchymoses. No pericarditis. Lungs: Both alike, voluminous; only the upper part of the upper lobe appeared normal. The rest was of a dull, light, muddy, red color throughout and showing small roundish gray spots. On feeling the tissue there was no crepitation noted, a feeling of solidity was everywhere manifest, pieces cut from these lobes sank at once in water. The cut surfaces were smooth and pus oozed out of cut bronchi in places. There were no signs of pleuritis and no ecchymoses.

MICROSCOPIC. *Liver.*—The organ is hyperemic and the blood everywhere contains a large number of round and polynuclear cells. The marked feature in the specimen is the general normal appearance of the cells but here and there throughout the section small, marked focal necroses, in many places no parenchymatous cells remaining, accompanied by infiltration of leukocytes of the round and polynuclear variety. The lymphatics of the portal canals are crammed with leukocytes. As a rule there is no destruction of bile ducts by the necrotic process; in one or two places such has occurred by the spread of the inflammatory reaction from a nearly necrotic focus in the liver substance.

Kidney.—Normal.

Lung.—Very edematous, alveolar cells desquamated in excessive numbers accompanied in a few places with a moderate number of white blood cells; as a rule these latter are everywhere scant in numbers. Hyperemia. No bronchitis, altho in bronchioles filled with fluid some of their epithelium has desquamated.

Spleen.—Very hyperemic. Malpighian bodies stand out sharp and normal.

Cat 7.—This animal was fed like Cat 6 with butter from New Mexico. The butter in this case was not definitely implicated in the production of illness, altho coming as it did from a region where milksickness prevailed it was regarded as possibly infectious. *B. lactimorbi* was found in the butter. The cat remained well.

Cat 8.—Fed with butter presumably concerned in the production of the outbreak of milksickness at Morris, Ill., November, 1908 (p. 416). Conditions of experiment as with Cat 6. *B. lactimorbi* found by culture to be present in the butter. Three doses of butter of 10 gm. each given in warm milk on January 16, 17, and 18. Weight January 18, 990 gm.; January 19, 985 gm.; January 20, 965 gm.; January 22, 880 gm.; January 23, 865 gm.; January 24, 820 gm.; January 25, 8–gm.; January 26, 765 gm.; January 27, dead. During this period there was little noticable change until January 24, when the cat, altho eating well, was noticed to be getting very weak. This was followed by rapid emaciation and death.

Autopsy.—A much emaciated animal. No subcutaneous fat. *Lung* partially collapsed, both alike in appearance. Lower lobes congested and showing a few scattered areas of bronchopneumonia; portions cut from congested areas float. No ecchymoses; no pleuritis. *Heart* apparently normal as were *all other* organs; the mucosa of the small intestine showed faint general injection; gut empty.

MICROSCOPIC. *Small intestine.*—Normal.

Kidney.—Cells almost everywhere have a peculiar hyalin appearance (faulty fixation).

Spleen.—Hyperemia and an increase in cells of spleen pulp. Malpighian bodies normal.

Lung.—The section in part shows collapse of the alveoli, accompanied by leukocytic invasion in two localities with bronchial involvement (bronchopneumonia). General hyperemia.

Liver.—General hyperemia accompanied by a leukocytosis. Parenchymal cells generally normal; here and there some lobules show fatty change and cloudy swelling; and occasionally are found very small foci of necrosis with accompanying leukocytic infiltration.

Cat 9.—Fed with a filtrate of a four-months-old asparagin-medium culture of *B. lactimorbi*; negative result.

Cat 10.—Fed with asparagin solution alone as a control; negative like Cat 9.

Lambs.—These animals were subjects of a feeding experiment extending over about three weeks. They were given gelatin cultures of two strains of *B. lactimorbi*, one from feces of A. McC., Altamonte, Ill., the other from the brain of J. Morrow's lamb (No. 1), Tiro, O. Through a mistake on the part of the attendant, both lambs were given mixtures of the cultures, so that independent pathogenicity of two strains was not established. No definite signs of illness were noted.

Lamb 1.—Male, about six months old, weight about 35 lbs. Chloroformed, and autopsied at once. There was little subcutaneous fat on reflecting the skin.

Thoracic cavity.—No abnormal amounts of fluid in either pleural sacs or pericardial sac. The thoracic viscera appeared quite normal.

Abdominal cavity.—There was no general peritonitis. The rumen evidently contained food as it was distended some; the other three portions of stomach seemed empty. The upper two-thirds of small intestine was empty and pale; venules distended with blood but showing no inflammatory condition. The lower one-third of gut, the cecum, and the colon contained fecal material.

In four places on the peritoneal surface of the lower one-third of the small gut were found yellow masses of fibrino-purulent nature about 4 mm. in diameter, with no signs of inflammation about them. These were smooth on top, and could be peeled off easily *en masse* from the tissue below without causing loss of substance. On account of its tough nature, and lack of inflammatory reaction about it, the exudate was considered old. Each cap of exudate was found to have underneath it, localized in the wall of the gut, an opaque, yellowish-gray, tough nodule. Other nodules could be seen and felt in other places in the gut and in the cecum without their being capped with old exudate. On opening the intestine, it appeared normal with the exception of the aforesaid nodules which were found to be imbedded in the submucosa, being covered with intact mucous membrane, and showing no evidence of present inflammation; the process seemed to be undergoing resolution. The colon was free of nodules and looked normal. The mesenteric glands were pale and enlarged and firm; one particularly large gland was found close to the portal vessels.

Liver.—The organ did not seem to be enlarged. On its upper surface but in the parenchyma were found two areas of a yellowish-gray color, about 1.25 cm. in diameter, projecting above the surface about 3 mm. in a nodular manner, capped with exudate similar to that seen on the surface of the small intestine, but in one spot being lightly glued to the diaphragm over an area roughly 4 cm. all around the nodule. The exudate was old and there were no signs of acute inflammation in or around the nodules. A similar nodule was found on the under surface of the liver near the free margin and 3 cm. to the left of the gall-bladder. The liver was of a deep red color before being incised and cut free; on bleeding it was found to be of moderately deep ochre color; the lobules could be made out, there was no evidence of fatty change, nor could there be said to be any very definite evidence of cloudy swelling, altho the consistency of the organ was less than normal. Gall-bladder normal. Spleen normal. Kidneys normal. Heart normal. Brain and meninges normal.

BACTERIOLOGY. *Agar-plate cultures* made from heart, liver (nodules and exudate above them), intestinal (exudate over nodules; portal gland). Coverslips from same locations excepting heart blood.

MICROSCOPIC. *Liver.*—(*a*) The whole section shows condition of cloudy swelling of mild degree associated with fatty metamorphosis; the fat granules being numerous within each cell, occasionally they are of large size and few in each cell. The degeneration is less marked in the outer zone of each lobule. The nuclei of the cells stain poorly or are absent. The enlargement of the cells almost obliterates the capillaries and there can be found here and there in-growth of connective-tissue cells in few numbers from the portal canals into the lobules; in other places it seems to arise from the capillary endothelium. In no instance is this proliferation more than barely noticeable. Central veins are well filled with blood altho little can be seen in the greatly compress capillaries. In places the capsule shows signs of inflammatory reaction with granulation-tissue formation. The liver cells for a short distance below the capsular reaction are extraordinarily increased in size and show cloudy swelling in marked degree.

b) This section was taken from around one of the necrotic foci; it shows a large irregular necrotic mass of tissue, which has a feeble architectural resemblance to liver substance in parts (contains broken nuclei, etc.) surrounded on all sides by active inflammatory tissue, made up of large numbers of round cells, fewer polymorphs, and a large amount of granulation tissue, some few multinuclear cells (not like tubercle) and new capillary vessels. The amount of liver substance in the section shows cloudy swelling with fatty changes, and there is marked round-cell infiltration and connective-tissue proliferation in the portal canals and apart from them in places. No bacterial masses (high-power dry lens) can be seen associated with the process, not even in one very small focus; there simply seems to be an acute focal necrosis, intense focal karyorhexis, and, outside of this, granulation-tissue formation more or less free of cellular infiltration but bounded by a dense zone of round cells.

Small intestine (section through nodule).—There is a generalized intense inflammatory reaction involving the mucosa of the whole circumference of the section, the villi being greatly thickened and swollen by the congested blood vessels and masses of round cells and occasional polynuclear leukocytes. There is great destruction of Lieberkühn's follicles in many places, in others infiltration with cells. The lymphatics piercing the inner muscular coat contain round and polynuclear leukocytes. In particular the inflammatory reaction is concentrated in three foci of acute inflammation accompanied by relatively extensive necrosis, two foci are close together, and the third a little distance away. They have arisen in the submucosa and each is surrounded by an actively proliferating zone of granulation tissue containing some round and polynuclear leukocytes, and beyond, greater numbers of these cells are located. The necrotic tissue seems to have been made up of round cells and proliferated connective-tissue cells. The inflammation in one place extends through the submucosa toward the lumen of the gut and is covered by a thin layer of mucous tissue devoid of any tubular structure; only a few shrunken villi remain and these are denuded of epithelium and are hyperemic. In another focus the inflammatory reaction has pushed through the muscular coats and has involved the peritoneum in acute inflammation. No bacterial masses can be made out by high-power dry lens.

In other sections taken where no nodules were found the gut is normal.

Heart (long. sect. vent.).—Everywhere the muscle retains its striations altho the fibers in many bundles do not take the stain well. There is a very general acute interstitial myocarditis as shown by the displacement of fibers by accumulation of large numbers of both round and polymorphonuclear leukocytes and proliferation of endothelial cells.

Kidney.—Acute parenchymatous nephritis affecting the convoluted tubes chiefly, in less degree the loops of Henle, whilst only occasionally the collecting tubules; fatty deposition seen in scant degree here and there. Colloid material seen now and then in some tubules. Necrosis of epithelium. The glomerules simply show evidence of hyperemia. There are no interstitial changes.

Lymph gland.—Hyperplastic and edematous.

Lamb 2, male, about six months old, weight about 28 lbs. Chloroformed at 3:20 P. M., and body examined at once. Conditions were practically same as in Lamb 1 excepting that there were fewer capped intestinal nodules, but more imbedded ones in the same regions and particularly in the cecum. The liver had only one surface nodule, but several internal foci or nodules which as in the former case showed no signs of active inflammation and were also tough to the knife. The consistency was much softer, the lobules could not be made out, and there was evidence of cloudy swelling, but no fatty change. Color a dark ochre.

The general impression received was that of an infection of the intestines and liver that had some time since passed the acute stage and had already advanced along one of general resolution.

Other organs as named in Lamb 1 were also found to be normal.

BACTERIOLOGY.—Cultures (agar plates) were made from heart blood, liver nodules, mesenteric gland, cecal submucous nodule, cecal feces, and purulent cap over cecal nodule.

Culture results, September 2:

Lamb 1. *B. lactimorbi* present in heart blood, and liver nodule (*abscess*); *Staph. albus*, portal gland; *Sterile*, exudates on liver and intestinal nodules.

Lamb 2. *B. lactimorbi* present in heart blood, cecal feces, exudate over cecal nodule, mesenteric gland, and in cecal nodule; Bacillus (undetermined),[1] liver nodule.

MICROSCOPIC. *Kidney.*—As for Lamb 1.

Liver.—Quite similar to section (*a*) Lamb 1. In addition there is a local perihepatitis nodular in character. The node is made up of granulation tissue, center necrotic, and necrosed portion apparently in the midst of a sero-purulent fluid. The granulation tissue contains round and polynuclear leukocytes and is surrounded with a zone of the same. The tissue on the extreme periphery of the focus of acute inflammation is edematous. A slight amount of the liver tissue has been involved in the inflammation, and certain of the liver cells near by seem to be undergoing proliferation, showing intense staining of nucleus, mitosis, dense staining of protoplasm.

Large intestine.—Great hyperplasia of solitary follicles accompanied by a very considerable degree of both round and polynuclear leukocytic infiltration of submucosa and mucosa, destruction and loss of columnar epithelium of tubules and tubules themselves in the inflammatory areas. Another section passes through a nodule in the walls of some portion of the large gut. The nodule appears to be a greatly hyperplastic solitary lymph follicle.

Pancreas.—Nothing abnormal detected.

Calf 1.—A calf (C. 1) weighing about 350 pounds, was fed with agar-plate cultures of *B. lactimorbi* at intervals of a few days during a period of about six weeks. To all appearances the animal remained entirely well and showed no characteristic symptoms, nor, indeed, symptoms of any kind. The animal was killed at 9 P. M., and the autopsy was held the next morning at half-past nine. The following pathological conditions were found:

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[1] Culture accidentally lost.

Heart.—A small ecchymotic spot was found beneath the epicardium of the right ventricle near the apex; the organ was otherwise in an apparently normal condition.

Liver.—On the surface in three or four places were found small areas of irregular shape of a uniform reddish-gray color in which the architecture of the liver substance could not be seen. These were considered to be necrotic in nature. On section, these areas seen on the surface were found to dip down into the parenchyma to varying depths, preserving the same features as seen on the surface. On further examination of the organ there was found in the posterior portion of the large lobe some 3 cm. below the surface an irregularly shaped necrotic mass of about 6 cm. in diameter, whose appearance corresponded entirely to that of the smaller areas just described: it was very friable, breaking down on the slightest pressure. In other respects the organ appeared normal.

Mesenteric glands.—These were generally much enlarged and less firm than normal. Other organs and tissues appeared to be in a normal state.

MICROSCOPIC. *Lung.*—Bronchial lymphatics crowded with round cells, no sign of tubercles. Lung otherwise normal.

Lymphatic gland.—Normal.

Spleen.—Apparently an increase in the fibrous-tissue elements of the organ.

Kidney.—Acute parenchymatous nephritis confined most largely to the convoluted tubules, and the ascending and descending loops of Henle, much less in the collecting tubules. The tubules contain both granular material and colloid droplets. There is glomerulitis also, with some desquamation of cells and collection of granular and colloid material within Bowman's capsule.

Heart.—Specimen shows normal tissue.

Liver.—Postmortem change only; invasion with *B. welchii.*

Colon.—Appears normal.

Calf 2.—Another animal (C. 2) was fed with spore-bearing cultures in a similar manner. Three days after the first feeding the feces were soft, unformed, and contained much mucus. When exercised by running the animal was readily fatigued and showed great unwillingness to move, altho on the preceding day it had been very active. On the fourth day the disinclination to muscular exertion was still more marked. There was much mucus in the feces, and microscopic examination showed the mucus to be filled with slender, granular-staining bacilli morphologically agreeing with *B. lactimorbi.* With the use of cultural methods *B. lactimorbi* was isolated and definitely identified. Nine days after the first feeding an abundance of blood-streaked mucus appeared in the stools. During the next two weeks little change was noted in the condition of the animal, beyond a slow but steady drop in the temperature, which after the first 10 days, ranged below 100° F. a large part of the time. Four weeks after the dosing was begun the animal was alive, but emaciated and rather stupid. At the end of another week while being led about the yard, the animal's forelegs seemed to give way suddenly and it went down on its knees with head on the ground, but did not lose its balance completely. After a while it struggled to its feet and moved on, only to repeat the performance a little later. This behavior strikingly reminded us of the cattle affected with "slows" or "tires," as we have seen them in the Pecos Valley, but there were no "trembles" in this case. The calf recovered and was chloroformed.

The autopsy was made at once. The only pathological condition found was confined to the small intestine which was covered with small hard nodules averaging in size that of a pea (some were about the size of shot); these were found along the whole length of the intestine but were more plentiful in the jejeunal portion. Some of the nodules were injected more or less deeply. The interior of some consists of a dry cheesy substance. The contents of the intestine were made of up much yellowish mucus and a little food material.

BACTERIOLOGY.—*B. lactimorbi* was isolated from the intestinal mucus and from the contents of a nodule, in the latter instance accompanied by a yellow coccus. The liver culture was sterile.

MICROSCOPIC. Alcohol fixation; hematoxylin and eosin. *Small intestine.*—Mucous membrane everywhere normal. Peritoneal covering thickened by increased growth of connective tissue, non-inflammatory. The section goes through a nodule which is made up of vascularized connective tissue showing no signs of any inflammatory change or degeneration; the peritoneum is everywhere intact.

Cerebrum.—Appears normal.

Kidney.—Poorly preserved.

Spleen.—Appears normal.

Cerebellum.—Appears normal.

Heart muscle.—Appears quite normal.

Liver.—Appears quite normal.

Lymphatic gland.—Quite edematous in its central portion, otherwise normal.

SUMMARY AND CONCLUSIONS.

There is no doubt that a disease exists under the name of milksickness, trembles, etc., which is common to man and some of the higher animals and is characterized by a fairly definite symptom-complex. This affection occurs occasionally at the present time in the states of North and South Carolina, Kentucky, Tennessee, Ohio, Illinois, Indiana, Michigan, and Texas, and in the territory of New Mexico. It has prevailed in the central western states for upward of a hundred years; from 1800 to 1840 it was quite common in certain districts altho the actual area affected does not seem to have been much if any greater than at present. Its reduction seems to have been brought about by the discovery that certain tracts of land were concerned in the production of the disease and that clearing, drainage, or cultivation of these tracts removed their dangerous qualities. "Milksick land" has also been fenced off from adjoining pastures known to be harmless.

The disease is usually contracted in the first instance by grazing cattle or sheep having access to the infected territory. It is communicated to man most frequently through the medium of raw milk or butter; meat also, especially if not thoroughly cooked, is thought to convey the disease. Carnivorous animals are liable to develop the malady when they feed on the carcasses of animals dead from trembles. Water is a possible source of the disease in both man and animals.

The course of the disease in cattle is marked by lassitude and muscular weakness sometimes, but not invariably, accompanied by constipation. There is often muscular twitching or trembling and occasionally signs of nervous excitement. The temperature in the mid-course and late stages of the disease is generally normal or subnormal.

In man there is as a rule excessive vomiting and obstinate constipation accompanied by great weakness. The temperature is normal or subnormal. A peculiar sweetish odor, which is also noticed in cattle and is due to acetone, is present in the breath and in the urine. The recorded mortality in man is about 20 to 25 per cent but owing to the fact that the severe cases have attracted most attention the actual mortality is probably much lower than this and is very likely less than 10 per cent. Relapses are rather frequent. Little if any immunity is conferred by an attack.

One of the main lesions found in the postmortem examination of cattle is fatty degeneration of the liver which is often very extreme. The small intestines are usually empty except for a tenacious yellow mucus. In some instances hyperplastic areas are noticed in the intestinal walls and occasionally small hard nodules are found. The mesenteric glands are often enlarged. The kidneys show as a rule cloudy swelling or fatty degeneration. We have found no involvement of the central nervous system. The heart muscle often shows fatty degeneration, sometimes in slight, sometimes in marked, degree. Ecchymoses on the wall of the heart, on the liver, and occasionally on the spleen are observed. The voluntary muscles do not seem affected.

In man the changes observed by us in the autopsy of a single fatal case are very similar to those found in cattle. Tissues from other fatal cases show microscopically extreme fatty degeneration of the liver, and a similar alteration or cloudy swelling in the kidney. We have found nothing resembling the profound disturbance of the central nervous system described by Graff.

Many different theories have been advanced to account for the origin and peculiar characters of the disease. Mineral poisons, such as arsenic and copper salts, have been conjectured to exist in certain soils in such quantities as to be taken up by forage plants which in turn are eaten by grazing animals. The poisonous substances are then supposed to be eliminated in the milk and to cause poisoning in man when the milk or milk products are taken into the alimentary canal. Analyses, however, have failed to reveal the presence of foreign mineral substances either in the suspected food substances, in the stomach contents or the tissues of affected animals, or in the soils of the incriminated regions. There is furthermore no correspondence between the underlying geological formations or the chemical composition of soils and the presence or absence of the disease. Adjoining tracts of pasture land to all appearances identical in character may on one side of a division fence give rise to milksickness, on the other be harmless.

Poisonous plants of various kinds have been held by observers to cause milksickness. There is no agreement, however, as to the responsible species. Plants firmly believed in some localities to cause the disease do not grow in other localities where the disease is quite prevalent. Feeding experiments with suspected plants have in no case given unambiguous results.

Living microorganisms or their products have been held to be the cause of the disease. According to the testimony of a number of observers the disease is self-propagating under some conditions and may be passed on without limit from one animal to another by the simple expedient of feeding one animal on the carcase of its dead predecessor. We have not ourselves been able to observe such a transfer, but our material has been very limited and observations of the disease under natural conditions show that transmission occurs very irregularly. It is also asserted that the virus of the disease is destroyed or weakened by heat in the same manner as that of various well-known infectious diseases. Observers agree that a single dose, and that not a large one, of affected milk or butter will produce the disease. Epidemiologically the correspondence of this disease with anthrax is very close.

From practically all cases of the disease that we have seen in man and other animals (horse, sheep, cattle) we have isolated an aerobic spore-bearing bacillus which grows well and characteristically on the ordinary culture media. We have found this bacillus—named *B. lactimorbi*—in the internal organs and heart blood of animals examined but a few hours after death. In some instances it was present in pure culture (e. g., heart blood of a heifer, liver of a fetal calf, gut nodule of a horse, etc.). The same bacillus has been found by us in cow's milk collected by one of us under aseptic conditions and in butter suspected of having communicated the disease. It was also present in the feces in several non-fatal human cases of milksickness. We have also found it in the soil of milksick regions. The force of such observations is weakened by the fact that a bacillus to all appearances morphologically and culturally identical has been isolated by us, not only from the soil of districts where milksickness prevails and on certain plants growing in those regions, but also from earth taken from places where the disease has never been known, and from normal cow feces.

When this bacillus is injected subcutaneously or intraperitoneally in pure culture into rabbits or guinea-pigs little or no effect is usually produced, altho in a few instances it has seemed to exert some pathogenic action. Fed in large quantities to these animals no deleterious action whatever is observed. On the other hand when fed in considerable quantities to dogs and cats symptoms and lesions are produced that are very similar to those observed in animals naturally affected with milksickness. In dogs, for example, a tendency to bronchitis is manifested (cf. McCall, 1822). The lesions in experimental animals in some respects resemble macroscopically and microscopically those observed in animals that have contracted the disease in a natural manner. Lambs fed with this bacillus showed nodules in the intestinal wall similar to those found in some naturally infected animals. From the majority of experimental animals *B. lactimorbi* was recovered, often in pure culture, from the various internal organs such as the liver, spleen, and kidneys. It was also found in abundance in blood-flecked masses of mucus voided by the dogs and calves under experimentation. Two calves and a horse fed with cultures have given generally inconclusive results.

Taken as a whole the facts do not surely indicate that a specific microorganism is the cause of milksickness or trembles. The bacillus in question belongs to a group which seems widely distributed and for the most part certainly not endowed with pathogenic qualities. In particular localities, however, where the soil conditions are favorable in respect to moisture and other unknown factors, strains of the bacillus perhaps possess pathogenic or toxigenic characters but if so, these, according to our experience, are quickly lost under artificial culture. It seems possible, judging from the observations of Mr. Luckhardt, which follow this paper, that *B. lactimorbi* is more commonly present on the surfaces of certain plants than on others but further observations will be needed to establish this fact.

The partly incomplete results and conclusions set forth in this paper are presented at this time with some hesitation, but the great rarity of material available for studying milksickness makes it desirable to record such facts as we have secured in the hope that they may be of use to other observers who chance across the malady from time to time.

BIBLIOGRAPHY.

ACHELOR, B. "Milk Sick," *Med. World*, 1884, 2, p. 141.

ALLEN, Z. "Milk-sickness," *Ill. Med. Rec.*, Vandalia, 1878–79, 1, p. 88.

ANDERSON, W. "Milk sickness and the Illinois Legislature," *Chicago Med. Jour.*, 1867, 24, p. 163.

BAILEY, F. K. "Milk sickness," *Trans. Ill. Med. Soc.*, Chicago, 1888, p. 45.

BARBEE, W. J. "Facts relative to the endemic disease called by the people of the west 'milk-sickness,'" *West. Jour. Med. and Surg.*, Louisville, 1840, 1, p. 178.

BEACH, W. M. "Milk-sickness," *Jour. Amer. Med. Assoc.*, 1883, 1, p. 71; also *Trans. Ohio Med. Soc.*, Columbus, 1884, 38, p. 125.

BECK, F. P. AND VIOLA. "Milk sickness: report of a case," *Chicago Clinic*, 1905, 18, p. 249.

BECK, J. C. "Milk-sickness," *N. W. Med. and Surg. Jour.*, Chicago, 1857, 14, p. 496.

BECK, L. C. "Facts relative to a disease generally known by the name of sick stomach or milksickness," *N. Y. Med. and Phys. Jour.*, 1822, 1, p. 315.

BENNETT, J. "Observations on the Sick stomach or Milk sickness, as it appears in certain parts of Kentucky," *West. Q. Reporter M. S. and Nat. Sc.*, Cincin., 1822, 1, p. 353.

BOGGS, T. R. "Milksickness," *Osler's Modern Medicine*, 1907, 3, p. 546.

BOLLINGER, O. "Zur Aetiologie des Milzbrandes," *Sitz. d. Ges. f. Morphol. u. Physiol. in München*, 1885, 1, p. 21.

BOWMAN, J. "Milk sickness," *Cincin. Lancet and Obsv.*, 1870, 13, p. 521.

BOYLES, E. W. "Milk sickness," *Chicago Med. Jour.*, 1865, 22, p. 139.

BREWINGTON, W. J. "Milk sickness," *Cincin. Clinic*, 1876, 10, p. 76.

Bridgeman, W. S. "Milk sickness," *ibid.*, 1876, 10, p. 68.

De Bruler, J. P. "Milk-sickness," *Chicago Med. Jour.*, 1858, 15, p. 206.

Buck, J R. "Remarks on the milk sickness, with cases," *Med. Exam.*, Phila., 1840, 3, p. 792.

Bürger. "Die Milchkrankheit der Nord Amerikaner," *Mag. f. d. ges. Heilk.*, Berlin, 1825, 18, p. 176.

Byford, W. H. "Milk sickness, poison, tires, etc.," *Nashville Jour. Med. and Surg.*, 1855, 9, p. 460; also *N. W. Med. and Surg. Jour.*, 1856, p. 32.

C. M. B. "Milk-sickness," *Homoeop. News*, St. Louis, 1892, 21, p. 246.

Campbell, J. L. "Milk-sick, or Sick Stomach," *Phys. and Surg.*, Ann Arbor, 1881, 3, p. 347.

Carney. "Report on Milk-sickness," *Proc. Med. Convention*, Columbus, O., 1847, p. 39.

Carpender, G. W. "Milk Sickness," *Med. World*, 1884, 2, p. 83.

Chamberlain, W. B. "Extracts from a dissertation on gastro-enteritis, commonly called sick stomach," *Ohio Med. Reposit.*, Cincin., 1826–27, 1, p. 1.

Chase, S. C. "The Cause of Milk Sickness," *Cincin. Lancet and Obs.*, 1861, 4, p. 347; also *Chicago Med. Jour.*, 1861, 18, p. 438.

Chesney, J. P. "Milk-sickness," *St. Joseph Med. and Surg. Reporter*, 1880–81, 1, p. 97.

Coleman, A. "Observations on the disease generally known by the name of sick-stomach," *West Q. Reporter, M. S. and Nat. Sc.*, Cincin., 1822, 1, p. 133; also *Phila. Jour. M. and Phys. Sc.*, 1822, 4, pp. 322, 331.

Collins, W. J. "Milksickness," *Med. Standard*, 1902, 25, p. 420.

Compton, J. W. "Milk-sickness," *Indiana Med. Reporter*, Evansville, 1881, 2, p. 249.

Conner, J. J. "A further contribution to the subject of milk-sickness," *Chicago Clinic*, 1904, 17, p. 333.

Converse, J. N. "Remarks on Milk-sickness and trembles," *N. Y. Jour. Med.*, 1853 (Ser. 2), 11, p. 358.

Cosby, A. D. "Pathology and Treatment of Milk-sickness," *Atlanta Med. and Surg. Jour.*, 1866–67, 7, B, p. 481.

Cox, E. T. "Influence of Geology on Local Diseases," Ref. in *Med. and Surg. Reporter*, 1881, 45, p. 49.

Crawford, A. C. "The Supposed Relationship of White Snakeroot to Milksickness or 'Trembles,'" 1908, *Bull. 121*, Bureau of Plant Industry, U. S. Dept. of Agri.

Crawford, J. "Remarks on Milk-sickness," *West. Lancet*, Cincin., 1843–44, 2, p. 135.

Crook, J. W. "Twenty propositions on Milk-sickness," *N. W. Med. and Surg. Jour.*, 1857, 14, p. 489.

Crooks, C. V. "Milk-sickness, its causes and treatment," *Med. and Surg. Reporter*, Phila., 1873, 29, p. 22.

Crookshank, N. "On the sick stomach of the western country, or gastro-enteritis," *Phila. Jour. Med. and Phys. Sc.*, 1826, 12, p. 252; also *Ohio Med. Reposit.*, Cincin., 1826–27, 1, p. 9.

Davis, C. W. "Treatment of Milk-sickness," *N. W. Med. and Surg. Jour.*, 1852–53, 9, p. 13.

Davis, K. H. "Milk-sickness," *Atlanta Med. Reg.*, 1881–82, 1, p. 391.

Dawson, J. "Causes and Treatment of Milksickness," *Proc. Med. Convention in Ohio*, Cincin., 1842, p. 45.

Dewey, J. S. "Milk-sickness," *N. W. Med. and Surg. Jour.*, Chicago, 1854–55, N. S., 11, p. 541.

Dickey, W. "An essay on Milk-sickness," *West. Lancet*, Cincin., 1852, 13, p. 390.

Dixson, M. L. "Milk-sickness," *Transylv. Jour. Med.*, Lexington, Ky., 1833, 6, p. 157.

Dorsey, G. V. "Remarks on a peculiar Epidemic Fever of Miami County, O.," *Western Lancet*, Cincin., 1847, 6, p. 76.

———. "Milk-sickness: A question of priority," *Clinic*, Cincin., 1876, 10, p. 100.

Drake, D. "Milk-sickness," *West. Jour. Med. and Surg.*, Louisville, 1840, 2, p. 80.

———. "A memoir on the diseases called by the people 'Trembles' and 'Sick Stomach' or 'Milksickness' as they have occurred in the Counties of Fayette, Madison, Clark, and Green, in the State of Ohio," *West Jour. Med. and Surg.*, 1841, 3, p. 161.

———. "Arsenic and the Trembles," *West. Jour. Med. and Surg.*, 1842, 5, p. 236.

———. "Northern limits of Milk-sickness," *ibid.*, 1843, 7, p. 65.

———. "The 'sick stomach' or 'milk-sickness' of the Western States ascribed to *Rhus radicans* by an unprofessional correspondent of the editor," *West Jour. Med. and Phys. Sc.*, Cincin., 1836, 9, p. 243.

Drake, D., and Yandell, L. P. "Milk-sickness, *alias* sick stomach; and its treatment," *West Jour. Med. and Surg.*, Louisville, 1840, 1, p. 84; 2, p. 80; 1841, 4, p. 75; 1842, 5, p. 235.

Dumm, S. C. "Epidemic gastritis or milk-sickness, or malignant malarial fever," *Cincin. Lancet and Clinic*, 1878, n. s., 1, p. 271.

———. "Milk-sickness treated with injections of brandy and milk," *Cincin. Lancet and Clinic*, 1879–80, n. s., 3, p. 209.

Dunglison, R. "Milk-sickness," *Cycl. Pract. Med.* (Tweedie), Phila., 1845, 3, p. 314.

Elder, E. S. "Morbeo Lacteo," *Tr. Indiana Med. Soc.*, Indianapolis, 1874, 24, p. 113.

Evans, J. P. "Milk-sickness, a mineral poison," *Nashville Jour. Med. and Surg.*, 1860, 18, p. 110.

Faux, W. *Memorable Days in America*, London, 1823, p. 212; see Thwaites, *Early Western Travels*, 11, p. 206.

Fisher, G. "Milk-sickness," *Chicago Med. Exam.*, 1861, 2, p. 538.

Flagg, E. "The Far West," p. 203; see Thwaites, *Early Western Travels*, 27, p. 95.

Ford, W. W. "Notes on Aerobic Spore-Bearing Bacilli, *Johns Hopkins Hosp. Bull.*, 1901, 12, p. 13.

Friedrich, L. "Zur Etiologie des Milzbrandes," *Dtsch. Ztschr. f. Thiermed.*, 1885, 11, p. 160.

Fulton, A. "Milk-sickness," *Cincin. Lancet and Observer*, 1873, 16, p. 641; also *Med. and Surg. Reporter*, Phila., 1884, 50, p. 449.

Gardner, J. "Milk-sickness: its microscopy," *St. Louis Med. and Surg. Jour.*, 1880, 38, p. 288; also *Indiana Med. Report*, Evansville, 1880, 1, p. 145.

———. "Milk-sickness," *Tr. Ohio Med. Soc.*, Cincin., 1887, 32, p. 81.

Graff, G. B. "On the milk-sickness of the West," *Amer. Jour. Med. Sc.*, Phila., 1841, n. s., 1, p. 351.

Gray, S. S. "Milk-sickness," *Ohio Med. Jour.*, Columbus, 1881–82, 1, p. 284.

HAINES, —. "Facts relating to the disease generally known as sick stomach," *West. Q. Reporter, M. S. and Nat. Sc.*, Cincin., 1822, 1, p. 141; also *Phila. Jour. Med. and Phys. Sc.*, 1822, 4, p. 331.

HENRY, A. G. "Milk-sickness," *West. Jour. Med. and Surg.*, Louisville, 1854 (4) s., 2, p. 25.

HESSLER, R. "Preliminary Note on an Almost Extinct Native Disease, Trembles or Milk-sickness," *Proc. Indiana Acad. of Sci.*, 1905, p. 122.

HIBBERD, J. F. "Observations on milk-sickness," *West. Lancet*, Cincin., 1844–45, 3, p. 445.

HOGG, S. "Fatal case of milk-sickness," *West. Jour. Med. and Surg.*, Louisville, 1842, 6, p. 253.

HORNE, J. "Remarks on milk-sickness," *West. Lancet*, Cincin., 1843–44, 2, p. 454.

———. "Miasmata the exciting cause of the disease called milk-sickness," *West. Lancet*, Lexington, 1846–47, 5, p. 397.

HOUSER, W. W. "Milk-sickness," *Amer. Med. Jour.*, St. Louis, 1880, 8, p. 445.

HOWARD, E. J. "Mukosma; Syro, milk-sickness, trembles, slows, tires, puking fevers, etc.," *Indiana Jour. Med.*, Indianapolis, 1871–72, 2, p. 370.

HURD, A. "Milk-sickness," *Clinic*, Cincin., 1875, 9, pp. 277, 290.

JACKSON, J. M. "Milk-sickness," *Louisville Med. News*, 1881, 12, p. 291.

JERRY, W. "The plant that causes milk-sickness," *Med. and Surg. Report.*, Phila., 1867, 16, p. 270.

JOHNSON, J. M. "Milk-sickness; its pathology and treatment," *Atlanta Med. and Surg. Jour.*, 1866–67, 7, p. 289.

JOHNSON, L. B. "Thoughts on Milk-sickness," *Richmond and Louisville Med. Jour.*, 1874, 17, 446.

JONES, G. W. "Upon the pathology of Milk-sickness." A thesis. *Chicago Med. Exam.*, 1862, 3, p. 267.

JONES, J. T. "A short essay on Milk-sickness (colica trementia)," *E. Tennessee Rec. Med. and Surg.*, Knoxville, 1852–53, 1, p. 321.

JORDAN, E. O., AND HARRIS, N. M. "The Cause of Milksickness or Trembles," *Jour. Amer. Med. Assoc.*, 1908, 50, p. 1665.

KENNEDY, J. F. "A reply to 'Z. Allen on Milk-sickness,'" *Ill. Med. Recorder*, Vandalia, 1878, 1, p. 146.

KENNICOTT, J. A. "Milk Sickness," *Chicago Med. Exam.*, 1861, 2, p. 538.

KIMMEL, J. A. "Milk-sickness in America," *Verhandl. d. x. inter. med. Cong., 1890*, Berlin, 1891, 2, p. 5; Abth., 48.

K——, H. M. "Milk-sickness," *Cincin. Lancet and Obs.*, 1862, 5, p. 21.

LANDRUM, Z. C. "*Rhus toxicodendron* (the cause of milk-sickness)," A review of an article on this subject by S. C. CHASE, *Atlanta Med. and Surg. Jour.*, 1861, 7, A, p. 1.

LAW, J. "Milk-sickness," *Vet. Jour. and Ann. Comp. Path.*, Lond., 1877, 5, p. 161.

LEA, W. W. "Cursory remarks on a disease vulgarly called milk-sick," *Phila. Jour. Med. and Phys. Sc.*, 1821, 2, p. 50.

LESCHER, J. J. "Milk-sickness," *Northwest. Med. and Surg. Jour.*, Chicago and Indianapolis, 1850–51, 7, p. 124.

LEWIS, J. T. "Cases of Milk-sickness, with some remarks on the treatment," *Transylv. Jour. Med.*, Lexington, Ky., 1829, 2, p. 241.

LOGAN, J. H. "The milk-sickness of upper Georgia and of other portions of the United States," *Atlanta Med. Reg.*, 1881–82, 1, p. 458.

LOGAN, J. M. "Essay on trembles, *alias* animal poison," *N. W. Med. and Surg. Jour.*, 1849–50, 6, p. 380.

LONG, S. H. *Account of an Expedition from Pittsburgh to The Rocky Mountain (in 1819–20)*, London, 1823, p. 76; see *Early West. Trav.*, 14, p. 141.

LYDAY, W. M. "Milk-sickness," *St. Louis Med. Era*, 1896–97, 6, p. 349.

MAUREL, —. "Swamp-sickness," *Dict. Encycl. d. sc. méd.*, Paris, 1884, 3 s., 13, p. 639.

MCANELLY, C. "Observations on Milk-sickness," *Transylv. Jour. Med.*, Lexington, 1836, 9, p. 88.

MCCALL, A. "An account of the diseased state produced by taking into the stomach the milk or flesh of cows, which has acquired deleterious properties from a vegetable sometimes eaten by those animals," *Phil. Jour. Med. and Phys. Sc.*, 1822, 4, p. 318.

———. "Observations on Milk-sickness," *Am. Med. Recorder*, Phila., 1823, 6, p. 254.

———. "Facts and observations on the milk-sickness, or sick stomach of Tennessee," *West. Jour. Med. and Phys. Sc.*, Cincin., 1830, 3, p. 465.

MCCLELLAND, J. S. "Reports on trembles, or milk-sickness," *Proc. Indiana Med. Soc.*, New Albany, 1854, —, p. 43.

MCCOY, G. W. "Milksickness," *Ann. Rept. of the Surgeon-General, Pub. Health and Mar. Hosp. Serv.*, 1907, p. 33.

M'KENNEY, T. L. *Memoirs, Official and Personal*, New York, 1846, p. 141.

MCNUTT, J. H. "Observations of milk-sickness," *Ill. and Ind. Med. and Surg. Jour.*, Chicago and Indianapolis, 1847–48, 4, p. 205.

MENDENHALL, I. "Milk-sickness," *Cincin. Lancet and Observer*, 1861, 4, p. 142.

Michigan State Board of Health, 1897, *25th Report*, p. 423; also 1905, *33d Report*, p. 201.

MILLER, W. B. "Pathology and treatment of milk-sickness," *Atlanta Med. and Surg. Jour.*, 1667–68, 8, p. 57.

MOSELEY, E. L. "The Cause of Trembles and Milk-sickness," *Med. Rec.*, May 15, 1909.

MURFIN, J. W. "Milk Sickness," *Med. World*, 1884, 2, p. 124.

NAGLE, I. E. "Milk-sickness," *Nashville, Jour. Med. and Surg.*, 1859, 17, p. 289.

NEWMANN, L. P. "Milk-sickness," *Chicago Med. Jour.*, 1867, 24, p. 253.

NICHOLS, J. H. "Milk-sickness," *Clinic*, Cincin., 1876, 10, p. 26.

NICOLAY, J. G., AND HAY, J. *Abraham Lincoln*, New York, 1890, 1, p. 30.

PALMER, G. T. "The recurrence of milk-sickness in Illinois," *Chicago Clinic*, 1904, 17, p. 267.

PATTON, J. C. "Milk-sickness," *Indiana Jour. Med.*, Indianapolis, 1875, 6, p. 139.

PHILIPS, N. F. "A case of milk-sickness," *Nashville Jour. Med. and Surg.*, 1876, 17, p. 61.

PHILIPS, W. H. "Milk-sickness," *Cincin. Lancet and Obs.*, 1877, 20, p. 130.

———. "Pathology of milk-sickness." *N. W. Med. and Surg. Jour.*, 1857, 14, p. 7.

PICKARD, J. "The pathology of milk-sickness in Parke county, Ind.," *N. W. Med. and Surg. Jour.*, 1857, 14, p. 260.

PRESTON, A. G. "Remarks on milk-sickness," *West. Lancet*, Cincin., 1843–44, 2, p. 264.

PUSEY, H. K. "Notes on Milk-sickness," *Louisville Med. News*, 1880, 9, p. 205.

———. "Milk-sickness," *ibid.*, 1880, 9, p. 16.

RAWLINGS, J. W. "Trembles in stock, and milk-sickness in man," *Tr. Drake Acad. Med.*, Evansville, 1874, 1, p. 50.

REAGAN, J. A. "Milk-sickness," *Med. World*, Phila., 1884, 2, p. 140.

REED, N. "The milk-sickness," *Boston Med. and Surg. Jour.*, 1856, 55, p. 273.

RUARK, S. "Milk-sickness," *Indiana Med. Reporter*, Evansville, 1880, 1, p. 262.

SAGER, J. "Milk sickness and its etiology," *Toledo Med. and Surg. Jour.*, 1879, 3, p. 137.

SALE, F. H. "Milk-sickness," *Cincin. Lancet and Obs.*, 1871, n. s., 14, p. 404.

SAWYER, A. "Milk-sickness; its cause and effects," *Med. and Surg. Reporter*, Phila., 1867, 16, p. 249.

SCHMIDT, C. H. "Milk-sickness," *Cincin. Lancet. and Obs.*, 1877, 20, p. 411.

SCHUCHARDT, B. "Die Milkkrankheit der Nord-Americaner," *Janus*, Amst., 1897–98, 2, pp. 437, 525.

SCOTT, H. "Milk Sickness," *Med. Compend.*, Toledo, 1889–90, 5, p. 137.

SEATON, J. S. "Remarks on a review of his essay on trembles, milk-sickness, etc.," *West. Jour. Med. and Surg.*, Louisville, 1842, 5, p. 64.

SHAPARD, J. C. "A few remarks on milk-sickness," *Nashville Jour. Med. and Surg.*, 1892, 71, p. 1.

SHARPLES, H. "Milk Sickness," *Eclect. Med. Jour.*, Cincin., 1875, 35, p. 410.

SHELTON, A. "Observations on milk-sickness," *Transylv. Jour. Med.*, Lexington, 1836, 9, p. 85.

SHORT, C. W. "Alleged causes of milk-sickness," *West. Jour. Med. and Surg.*, Louisville, 1840, 1, p. 231.

SHORT, H. S. *Eclect. Med. Jour.*, Cincin., 1875, 35, p. 211.

SIMON, R. J. "Milk-sickness," *Eclect. Med. Jour.*, Cincin., 1888, 48, p. 256.

———. "Milk Sickness," *ibid.*, 1875, 35, p. 66.

SIMPSON, D. S. "Extract from an inaugural thesis on milk-sickness," *Transylv. Jour. Med.*, Lexington, Ky., 1839, 12, p. 146.

SLACK. "Ergodeleteria," *West. Lancet*, Cincin., 1854, 15, p. 140.

SMITH, C. H. "Milk-sickness," *Phila. Med. Times*, 1874–75, 5, p. 186.

——— "Milk-sickness," *Boston Med. and Surg. Jour.*, 1867–68, 77, p. 471.

SMITH, J. N. "On milk-sickness," *Transylv. Jour. Med.*, Lexington, 1837, 10, p. 236.

SPALDING, J. "Milk-sickness," *West. Med. Reporter*, Chicago, 1881–82, 3, p. 266.

SUTTON, G. "Preliminary report on Milk-sickness as it prevails within the state of Indiana," *Proc. Indiana Med. Soc.*, Indianapolis, 1853, p. 176.

SWAN, I. S. "Milk-sickness," *West. Lancet*, Cincin., 1852, 13, p. 671.

SYKES, R. D. "Milk-sickness," *Columbus Med. Jour.*, 1891–92, 10, p. 65.

S———. "Alleged causes of the milk-sickness, or sick-stomach," *Transylv. Jour. Med.*, Lexington, 1829, 2, p. 145.

TAYLOR, G. B. "Facts and conjectures on the Trembles and Milk-sickness," *West. Jour. Med. and Surg.*, Louisville, 1842, 6, p. 181.

THOMPSON, S. "Milk-sickness or trembles, "*St. Louis Med. and Surg. Jour.*, 1848–49 6, p. 220.

THOMPSON, S. W. "On milk-sickness; its etiology and treatment," *West. Jour. Med. and Surg.*, Louisville, 1853, 3d s., 11, p. 471.

———. "Milk-sickness," *N. W. Med. and Surg. Jour.*, Chicago, 1853, 10, p. 225.

———. "An essay on milk-sickness," *ibid.*, 1854, 11, p. 385.

TOWNSHEND, N. S. "Milk-sickness," *Jour. Comp. Med. and Surg.*, N. Y., 1883, 4, p. 117.

TRAVIS, J. "Observations on milk-sickness," *West. Jour. Med. and Surg.*, 1840, 2, p. 101.

TROY, —. "A case of milk-sickness," *Cincin. Lancet and Obs.*, 1861, 4, p. 283.

TULLER, W. N. "Milk-sickness," *N. Amer. Pract.*, Chicago, 1889, 1, p. 402.

VAUGHAN, V. C. *Ptomains, Leucomains, Toxins, and Antitoxins* by VAUGHAN AND NOVY, Phila., 1896, p. 104.

WAGGONER, F. R. "Milk-sickness; its etiology, pathology, diagnosis and treatment," *Penins. and Indep. Med. Jour.*, Detroit, 1858–59, 1, p. 658; *ibid.*, 1859–60, 2, p. 5.

WAGMAN, J. W. "Morbid anatomy of Milk-sickness," *West. Jour. Med. and Surg.*, Louisville, 1841, 4, p. 234.

WALKER, J. W. "Milk-sickness," *Science*, N. Y., 1886, 8, p. 482; also p. 540 ref.

WALSH, W. E. "Clinical Report of the Reappearance of the Once Common and Fatal Milk Sickness or 'Milk-Sick,' with Successful Rational Treatment Deducted from Clinical Findings," *Ill. Med. Jour.*, 1909, 15, p. 422.

WAY, J. H. "The clinical history, nature, and treatment of milk-sickness," *Amer. Jour. Med. Sc.*, Phila., 1893, n. s., 106, p. 307.

WHITE, C. "Observations on milk-sickness," *Transylv. Jour. Med.*, Lexington, 1836, 9, p. 87.

WILKINSON, G. W. "Etiology of Milk-sickness," *N. W. Med. and Surg. Jour.*, Chicago, 1857, 14, p. 151.

WILLIAMS, J. A. "Milk-sickness," *Cincin. Med. and Surg. News*, 1863, 4, p. 167.

WINANS, M. "Practical observations on the disease denominated milk-sickness or sick-stomach," *West. Jour. Med. and Surg.*, Louisville, 1840, 1, p. 190.

WOOD, G. B. "Treatise on the Practise of Medicine," 1858, 1, p. 462.

WOODFIN, H. G. "Milk-sickness," *N. C. Med. Jour.*, Wilmington, 1878, 1, pp. 13, 137.

WOZENCRAFT, O. M. "Trembles and Milk-sickness," *Pacific Med. and Surg. Jour.* San Francisco, 1873–74, 16, p. 172.

WRIGHT, G. W. "Observations on the atmospheric origin of the Endemic, Sick-Stomach of particular situations in the Western States," *West. Med. and Phys. Jour.*, Cincin., 1827–28, 1, p. 369.

WRIGHT, G. W., AND BENNETT, J. "Proposals for publishing by subscription a treatise on the endemic sick stomach of the Western States," *West. Med. and Phys. Jour.*, Cincin., 1827–28, 1, p. 477.

YANDELL, L. P. "An essay on milk-sickness," *Transylv. Jour. Med.*, Lexington, 1828, 1, p. 309.

———. "Milk Sickness," *West. Jour. Med. and Surg.*, 1841, 4, p. 75.

———. "An inquiry into the nature of the disease called milk-sickness, *West. Jour. Med. and Surg.*, Louisville, 1852, 3, s., 9, p. 374.

"Report of Committee on milk-sickness," *Proc. Kentucky Med. Soc.*, Louisville, 1867, p. 88.

"Disease, A, in Ohio ascribed to some deleterious quality in the milk of cows," *Med., Reposit.*, N. Y., 1812, 15, p. 92.

"Milk sickness," *Maryland Med. and Surg. Jour.*, Balt., 1839–40, 1, p. 133.

"Milk-sickness or sick stomach," *West. Med. Gaz.*, Cincin., 1832–33, 1, pp. 101, 117.

"Milk-sickness, or trembles," *Proc. Ill. Med. Soc.*, Chicago, 1851, 1, p. 33.